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THE DIABETIC SITUATION IN MASSACHUSETTS

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BOSTON

THE long range problem which the diabetes of today presents is not recognized. And this is not strange because the outlook for diabetic patients has changed so much in a generation and even more markedly in the last fifteen years. When I[1] delivered the Shattuck Lecture in 1922 I showed that the duration of life of my fatal patients had risen on the average from 4.8 years prior to 1914 to 6.0 years between 1914 and 1922, a gain which then seemed remarkable because it was 25 per cent. For individual instances in which this figure was exceeded during the earlier decades of life I was forced to be content with a few examples. In fact, there were only 23 per cent before 1914 and 31 per cent between 1914 and 1922 who lived more than six years. As for patients exceeding the normal expectancy of life at the age of onset of their diabetes, it was almost unknown. To be sure, children nearly doubled their duration of life in the second as compared with the first period, but even then it was only 2.7 years, yet this gave a hint for the future. But even with the greatest optimism at that time, I did not imagine that the expectancy of life of a diabetic child of ten would advance to more than thirty-two years by 1938, that for ages under forty there would be 843 (623 living, 220 dead) of my patients, including 112 children, who had survived fifteen years of diabetes, or that for all ages there would be approximately 400 patients who had lived longer with the disease than they were expected to live without it.

What does this increasing duration of diabetes signify? It indicates that owing to the increasing duration of diabetes alone there are more than three times as many diabetic patients in Massachusetts as there were fifteen years ago. Incidentally, one might add that the average diabetic patient consulting a doctor today will probably live longer than that doctor will continue to practice medicine.

Read at the annual meeting of the Massachusetts Medical Society, Boston, June 2, 1938.

In 1937 the April, May and June number of the *Commonhealth* was devoted to a discussion of diabetes. This can be obtained on application to the Massachusetts Department of Public Health.

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DIABETIC MORTALITY IN MASSACHUSETTS

Diabetic mortality continues to rise in Massachusetts although with lessening velocity. It is true that in 1920 the crude rate per 100,000 was 20.6 and in 1937 it was 34.4. These figures, however, give a wrong idea because they are crude mortality rates and not figures adjusted for sex and age. When one remembers that diabetes is twice as frequent after the age of forty, it is obvious that if there has been a change in the number of individuals above forty, this must have a considerable effect on crude mortality figures.

Table 1. *Percentages of Population Attaining the Ages of Fifty and Sixty-Five Years.*

PLACE AND YEAR	PERCENTAGE ATTAINING FIFTY YEARS		PERCENTAGE ATTAINING SIXTY-FIVE YEARS	
	MALES	FEMALES	MALES	FEMALES
Massachusetts				
1900-1902	55.1	59.3	36.5	41.8
1920	66.6	69.2	47.1	50.9
1929-1931	75.4	79.1	53.0	60.1
United States				
1929-1931	74.5	78.8	53.1	60.6
1936	76.4	81.5	53.8	63.8

Through the courtesy of Dr. Herbert L. Lombard, of the Massachusetts Department of Public Health, and Mr. Herbert H. Marks, of the Statistical Department of the Metropolitan Life Insurance Company, I am able to present three tables which materially help in the elucidation of this question.

Table 1 shows the percentages of individuals in Massachusetts and the United States attaining the ages of 50 and 65 in various periods, according to sex. Thus, in Massachusetts between 1900 and

1902 only 55.1 per cent of men reached the age of 50 but by 1929 the percentage had increased to 75.4, and the increase in percentage of those attaining the age of 65 was almost as much. Women lived longer than men in the earlier periods but their increase in longevity is proportionately not so great. The increases, however, are so marked that it is evident if we are to form a conclusion as to whether diabetes is actually increasing, we must depend on mortality rates adjusted for sex and age. Sex is quite as important as age because at the higher ages the disease is much more frequent in women than in men.

23 per cent for men but of a decrease of 3.2 per cent for women. After 59 years the increase for both sexes is 25.9 per cent and essentially the same for both men and women; and this is different from the experience encountered generally elsewhere.

For 1936 the mortality rate per 100,000 in Massachusetts did not rise above 1.2 for the ages up to 19 years inclusive, between 20 and 39 years it lay between 2.0 and 3.1; between 40 and 49 years, 11.4; between 50 and 59 years, 51.6; between 60 and 69 years, 152.3; between 70 and 79 years, 309.6; and over 80 years, 286.5.

Table 2. *Standardized Death Rates per 100,000 from Diabetes Mellitus in Massachusetts by Sex and Age, with Percentage Changes in 1934-1936 from 1929-1931.*

Age Groups	1929-1931			1934-1936			Percentage Changes		
	Both Sexes	Males	Females	Both Sexes	Males	Females	Both Sexes	Males	Females
All ages	18.1	12.7	23.5	21.3	15.3	27.2	+17.7	+20.5	+15.7
Under 20	1.4	1.3	1.5	1.0	1.1	0.8	—28.6	—15.4	—46.7
20-39	3.1	3.1	3.1	3.0	3.2	2.7	— 3.2	+ 3.2	—12.9
40-59	25.9	17.4	34.2	27.4	21.4	33.1	+ 5.8	+23.0	— 3.2
Over 59	161.6	118.2	198.1	203.5	147.0	251.1	+25.9	+24.4	+26.8

Table 2 shows the standardized death rates per 100,000 from diabetes in Massachusetts by sex and age, with the percentage changes in 1934-1936 from 1929-1931. It is evident that for the 1929-1931 group under twenty the percentage decrease in the death rate is marked—28.6 for both sexes, 15.4 for men and 46.7 for women. Even in the 20-39 year group the fall for both sexes combined

Table 3. *Crude and Standardized Death Rates per 100,000 from Diabetes Mellitus.*

Group	1910		1920		1937	
	Crude	Standardized	Crude	Standardized	Crude	Standardized
Massachusetts	17.0	16.9*	20.6	19.3*	34.4	24.3*
United States Registration area	14.9	14.7	—	—	23.7§	19.2§
Registration states of 1920	—	—	16.1	15.2	24.2†	19.3†
Metropolitan Life Insurance Company, Industrial Department (ages 1-74)	13.1**	15.1**	13.6	15.6	24.8	20.6

*Adjusted to Mass. 1900.
§1936.
†1934.
**1911.

continues, 3.2 per cent, although for men there is an increase of 3.2 per cent counterbalanced by a decrease for women of 12.9 per cent. In the 40-59 year group the increase, 5.8 per cent, is peculiar in that it is made up of an increase of

For comparison, figures are given in Table 3 for three years, 1910, 1920 and 1937, both for the crude and standardized death rates per 100,000 from diabetes mellitus for Massachusetts, the United States and the Metropolitan Life Insurance Company. A study of this table shows that diabetes is increasing in all three groups, but the increase is very much less marked than the crude rates would lead us to believe; in fact, during the last six years the adjusted rate for policyholders in the Industrial Department of the Metropolitan Life Insurance Company has only increased from 20.5 to 20.8.

From a different angle, the change in the diabetic picture is evidenced by comparison of the average age at death of my diabetic patients between 1922 and 1936. For men it advanced ten years to 64.5, and for women, seven years to 66.0.

The number of living diabetic patients in Massachusetts was estimated by Bigelow and Lombard[2] in 1931 as 15,000. Today there are more. This is due partly to the new cases developing because of the aging population of the State and partly to increasing accuracy of diagnosis, but more especially to the great increase in the duration of the disease. An estimate of the present number of cases can be only approximate, but after discussion of the problem with my friends, Dr. Lombard and Mr. Marks, I should think it very likely that there are at least 18,000 or 20,000 known diabetic patients in Massachusetts.

THE EXTRAORDINARY DECLINE IN THE MORTALITY OF DIABETIC CHILDREN

The sharpest contrast in the diabetic population between 1922, just before the introduction of insulin therapy, and today relates to the children. Then they were few but now they are numerous, simply because they have ceased to die in childhood. No evidence exists to show that more children develop diabetes now than in years gone by, and with the falling birth rate the source of new diabetic recruits in Massachusetts and in the country as a whole is actually being reduced. In 1922 the birth rate in Massachusetts was 22.2 per 1000 but in 1936 it had fallen to 13.9. It is said for the United States as a whole there are 1,600,000 fewer children under ten than there were five years ago. Therefore in planning for the treatment of diabetic patients it is probably safe to say that we have as many children now as we will have in the future unless there is an increase in immigration or the birth rate rises. This has become plainly evident to Dr. Priscilla White and me in the last few weeks in planning for entries to camps for diabetic children. Last year some 212 were accommodated, and the prospect is that there will not be any considerable increase in applicants for 1938 or lack of accommodation unless one provides a longer stay in camp for each child than the two weeks allowed a year ago. In 1922 the children were so feeble that for most of them life was pure invalidism, and one never even thought of sending them to camp. Today they are so active and healthy in appearance that with few exceptions they cannot be distinguished from normal children of similar age.

The elimination of fatalities from coma is the chief reason for the prolongation of the lives of diabetic children. When children lived only a year the annual death rate was practically 100 per cent or 1000 per 1000. Between 1914 and 1922, in my own series, it had dropped to the rate of 362 per 1000, but between 1929 and 1936 the mortality among the children has varied between 12.2 and 9.7, depending whether we based it on children with onset of the disease prior to this period or in the period itself.

PROBLEMS CONFRONTING DIABETIC CHILDREN

The problems which confront the diabetic children of today were unheard of in 1922 largely because the children lived for so short a period. One can be sanguine about their solution because so often they are related to neglect in following treatment, to lack of intimate supervision or to treatment which is recognized today as imperfect. The great majority of the children are in excellent condition and quite free from complications, although with increasing duration of the disease such become manifest, and notably so in those who are frankly negligent. Of the few deaths which occur in children after five, ten or more years of the disease, coma still persists as a major cause, but tuberculosis is close to it, particularly in children with diabetes of long duration. The serious complications which are most apparent are deficient growth, — actual dwarfism, — which occurs in an appreciable number, hepatomegaly, which has been common until the advent of protamine insulin, and the whole train of complications one sees in neglected diabetes in adults — neuritis, defects in the eyes, arteries and skin, and not infrequently, especially in girls, infections of the genitourinary tract.

From the social standpoint arises the problem of advice as to the choice of a career and marriage; the latter will be discussed later. As to the former the limitation which my colleagues and I feel very real is the avoidance of contacts with tuberculosis such as are common for nurses and doctors. At present we discourage the entrance of diabetic patients into the nursing and medical professions.

We find that individuals with diabetes are becoming more numerous in our state sanatoriums for tuberculosis. The average number of diabetic patients in Massachusetts sanatoriums in 1937, according to information kindly furnished by Dr. Alton S. Pope, was 30, which is twice that of 1934, but practically the same as that for 1935 and 1936. The highest percentage of diabetic patients to the total sanatorium populations was 1.48. Of the 1024 patients admitted to my service for the first six months of 1938 there were recognized 6 cases with active tuberculosis — 4 patients showing tubercle bacilli in the sputum — with ages ranging from twenty-three to seventy-six. But I can say in contrast that of 104 deaths among 1063 patients since August 7, 1922, whose onset of diabetes was in childhood, 69 died of coma and 9 of tuberculosis, and of those who succumbed between ten and fifteen years after the onset of diabetes the percentage of tuberculous deaths to total deaths ran as high as 40, that is, 4 out of 10 cases.

HEREDITY, MARRIAGE AND THE PREGNANT DIABETIC PATIENT

Heredity was not mentioned in 1922 in the Shattuck Lecture. It was recognized, but its importance not realized. At that time practically no diabetic patients married, and if they did, the marriage was sterile, due usually to lack of fertility, seldom by design. There were a few exceptions. Pregnancy in women developing diabetes after one or more pregnancies was relatively

uncommon, but even with these patients the course was usually stormy and at least half the children were lost. Dr. Priscilla White[3] has found 130 pregnancies among our group in the twenty-four years prior to 1922, in contrast to Naunyn[4] who, in 1906, recorded having seen but one pregnant diabetic woman and to Bouchardat[5] who wrote in 1875 that he had not seen a single one. How great the difference today is evident from the fact that in the first six months of this year 28 of our patients reported themselves to be pregnant. Therefore it is appropriate to discuss the question of pregnancy for a diabetic patient, and its effect on mother and child.

I think no one would advise two diabetic patients to marry and have children, yet if a group of diabetic couples did disregard the advice, the outcome would not be quite so appalling as one might conclude at first thought. To be sure, all the children would have diabetes provided they lived to the respective ages at which, by statistical evidence, they would develop it. As a matter of fact, however, only about 44 of each 100 would do so, and of this number, approximately one third would acquire it below the age of forty, one third between forty and fifty-five and the remainder after fifty-five. Thus the outcome would not be so dreadful after all. Indeed one is tempted to look at it from an opposite point of view. Thus if all these pregnancies were avoided or terminated 2 healthy individuals below the age of forty would be sacrificed to avoid 1 with diabetes and 1 of the 2 remaining would be free from the disease until past fifty-five.

If one with diabetes marries one without the disease, the chances of the offspring's developing diabetes are reduced materially and, theoretically, if there is no heredity on the non-diabetic mate's side of the family, it would fall to zero. However, statements of this character are unreliable because in the United States presumably one fourth of the population, or something over 30,000,000, have a diabetic heredity element. From these considerations, therefore, I think one must be very cautious before telling a diabetic patient that he or she shall not marry and produce children. Particularly is this true when we realize the falling birth rate generally. If we should carry our plan to the extreme and prevent those with diabetes from having children, think of the quality and quantity of the inhabitants remaining, many of whom are far less fitted than those with diabetes to have them, and consider to what results a policy of this kind might lead. Diabetes it is true is hereditary and eugenically, although not practically, preventable. However, diabetic patients are so outstanding mentally and physically that I believe the world would be the loser without them.

The mortality of diabetic mothers has now been reduced so low that the risk resulting from a diabetic woman's becoming pregnant is not very much greater than that of a normal individual, provided the former can have care and close supervision throughout the entire pregnancy, particularly during the last four months. Yet it is true that the danger is greater than for the normal woman and in unskillful hands can become considerable. One of the contributing causes is the frequent necessity for cesarean section in diabetic primiparas, which in itself carries a definitely increased mortality.

The mortality of the fetus is considerable and especially so if we link with it the mortality of the infant in the first few hours following delivery. I suspect that if we could collect accurate statistics we should find that 50 per cent of all pregnancies in diabetic patients end in the death of the child, and even in the best of hands, it would be seldom that 85 per cent of the pregnancies resulted in living children. Obstetricians do not come in contact with such patients in the early stages of pregnancy and so are not in a position to give satisfactory or extensive data. I am in hope, however, that obstetrical societies will become so interested in this growing problem that statistics far more extensive than those collected by our group will soon be available. Only in this way can proper decisions be made regarding treatment of the mother and of the child.

DIETS

The diabetic diet today is characterized by its simplicity. Oddly enough today's average diet is approximately the same as the maximum diet which I advocated in 1922—carbohydrate 150, protein 70, fat 80 gm. The composition of this diet is so simple that it can be taught to a class of patients in a little over five minutes. Roughly it consists of three slices of bread, a large portion of oatmeal, three oranges, four portions of 5 per cent vegetables, ¼ pt. each of milk and cream, an egg, two moderate portions of meat, and three portions of butter. It is shown in Table 4. In case of illness it is a simple matter to change the diet to 1 qt. of milk, three slices of bread, one and a half portions of butter, one egg, one-half cup of cooked cereal, and two glasses of orange juice.

This is not the place for expanding on the details of this diet because that has been done elsewhere, and indeed, they are probably familiar to you. The simplicity of this diet is its characteristic. Obviously one can increase it or de-

crease it according to the age, weight and activity of the patient. If the patient cannot remain sugar-free on this diet or a similar diet adapted to his age, weight and activity, insulin in one of its various forms is indicated.

EXERCISE

In 1922 I did not mention exercise in my paper, because I understood so little about it that I was afraid to advocate it. Today we know it is of great value and a fundamental principle in the treatment of diabetes. In the mild case, exercise will lower the blood sugar and favor the utilization of carbohydrate. On the other hand, in the severe case it raises the blood sugar and can bring on acidosis and death. However, insulin has changed all this, and patients with severe diabetes taking insulin can show a fall of blood sugar equivalent to that of a normal individual; in fact we know that they will continue to store glycogen in the liver, muscles and skin like a normal individual. Exercise, protected by insulin, is a major factor in the treatment of diabetes today and is utilized by all patients except in the presence of infection. Without exercise diabetic college boys do less well than with it, and athletic coaches know that the diabetic patient can be utilized on major college teams just as are those without diabetes.

INSULIN

Practically all the changes in the situation in regard to those with diabetes which have taken place in the last half generation can be attributed to the discovery of insulin. The most spectacular achievement resulting from it undoubtedly is the reduction and almost complete abolition of coma.

Next to the prevention of acidosis I should say the greatest advantage from insulin to the diabetic patient is the power it gives him to work and to lead an essentially normal life, including marriage and the creation of a home. Prior to the discovery of insulin I cannot recall more than one or two instances in which diabetic patients married. Since its discovery a great many such instances have come to my attention, and it has been extraordinarily rare that the marriage has proved to be an unhappy one. These facts speak for themselves.

So far as I am aware there is no surgical problem which cannot be carried out on diabetic patients, but they are prone to surgical complications. Preventive surgery is often indicated and far more so than in normal persons. Thus with slighter signs and symptoms a tonsillectomy or appendectomy is performed, gall stones removed or thyroid disease attacked. Insulin has made surgery possible, but it has done something far more. It has brought the surgeon and the doctor into intimate daily contact and into mutual trust in the work of each other. Moreover, it has emphasized, and I should even say necessitates, the desirability of what I believe Eliason,[6] of Philadelphia, called one-man surgery. In 1922 the idea was becoming current that each surgeon in a hospital could not expect to operate successfully on diabetic gangrene any more than each member of a baseball team could serve as pitcher on a baseball nine in the course of a single game and anticipate a victory. Diabetic surgery also has helped the practice of surgery generally by directing attention to the value of appropriate anesthesia. Incidentally, it has advanced the profession of chiropody. If I should have advocated sending diabetic patients to chiropodists sixteen years ago I wonder what the members of the Massachusetts Medical Society would have said; yet today all of us recognize our indebtedness to chiropodists, and I believe the feeling is mutual.

Not the least of the advantages of insulin has been the recession of quacks and quack remedies in the treatment of diabetes. He is a very bold quack who would tell a mother to take away a dose of insulin from a child and replace it with a quack medicine. When Dr. Frederick M. Allen, of New York City, started the practice for diabetic patients to examine their own urines he began

Table 4. *Basic Diet for Cases of Diabetes Mellitus.*

Food	Amount	Grams in Each Unit				Grams in Total Amount			
		Total	C	P	F	C	P	F
Bread	3 slices	30	18	3		54	9	2
Oatmeal	1 large portion	30 (dry)	20	5	2	20	5	2
Orange	3	150	15			45		
Vegetables 3-5%	4 portions	150	5	2½		20	10	
Milk	¼ pt.	120	6	4	4	6	4	4
Cream, 20%	¼ pt.	120	4		24	4	4	24
Egg	1			6	6		6	6
Meat	2 portions	60		16	10		32	20
Butter	3 portions	10			8			25
				Total grams (approximate)		150	70	80
				Calories per gram		4	4	9
				Total calories		600 + 280 + 720 = 1600		

to sound the death knell of quackery. It is true that quackery still exists and occasionally I still run across its death-dealing influence resulting in diabetic coma, but quackery in the treatment of diabetes is no longer fashionable. For a doctor of today to give a proprietary medicine to a diabetic patient is a serious blunder.

PROTAMINE INSULIN

Already in various places and on many occasions I[7] have discussed protamine insulin, and by protamine insulin I mean protamine-zinc insulin. Recently I have followed up the first 1250 patients to whom I administered it and am engaged in the analyses of the replies. The indications are that at least 90 per cent of those who expressed an opinion are satisfied with it, and the majority of this group are very, very grateful for it. The remainder have had difficulties which are generally surmountable and merit discussion by themselves; this I shall undertake during this summer. Here is a letter from the mother of a diabetic child, which is typical of the majority of the answers I have received:

> Betty [Case No. 12809], who is now twelve, is better than she has ever been! The new insulin, protamine zinc, which she has been taking now for over a year, has meant the greatest improvement. She never has a reaction and is much more stable; in fact, she is so normal in every way that I forget she has diabetes. Taking it but once a day means a great deal psychologically, as you know she was taking the old insulin three times a day. Now, she can take it before breakfast and forget it.
>
> She got along beautifully last summer in Europe,—being gone two months,—and this year we hope to take her to a ranch as she is so particularly fond of horseback riding.

In summarizing the advantages of protamine insulin in connection with our scientific exhibit with the Metropolitan Life Insurance Company, we all agreed on the following: (1) treatment is simpler; (2) control is better; (3) patients are happier; (4) coma is lessened; (5) hepatomegaly is corrected; (6) lipodystrophy is less; (7) reactions are less frequent and usually less severe; (8) children grow and develop better.

Protamine insulin can be advocated today for all new patients and usually for old patients unless they have been habituated for years to the employment of regular insulin. With such, one must still be wary, and unless they can be under the closest supervision in their homes, they should enter the hospital for a week or ten days, be studied and a decision reached whether they are suitable for transfer from their regular insulin, which generally has worked well but has been inconvenient, to the protamine insulin, with which they are unfamiliar and may have difficulties for some weeks during the adjustment period. I always hesitate to disturb the course of a patient who is doing well. Moreover, all of us can be certain that new developments in the treatment of diabetes and in the manufacture of insulin will take place; any day we may have available a method or a product which will be of still greater advantage.

The action of protamine insulin is slow and sure and may be prolonged for as long as forty-eight hours. Therefore, meals must be spread apart and in general kept constant, often lunches of varying composition introduced in the forenoon, afternoon and on retiring, and perhaps the whole day's schedule more or less readjusted. In the end the patient receives insulin once a day, and to most that makes worth while the period of prolonged trial and error that is required to learn how to employ protamine insulin.

I confess I cannot tell in advance the patients who will do well or poorly with protamine insulin. Perhaps I have been negligent in the study of insulin-sensitive and insulin-insensitive individuals, and I am perfectly willing to encourage a renewal of efforts along these lines. I am aware that others[8] have found that insulin-sensitive patients do not react so well with protamine insulin as do those who are insulin-insensitive.

The patient taking protamine insulin may not be as nearly sugar-free throughout the twenty-four hours as he was when taking three or four doses of regular insulin each day. I feel that if the loss of sugar in the urine can be restricted to 10 per cent of the carbohydrate in the diet this is justifiable under present methods of treatment. The dosage of protamine insulin should be changed gradually, based on the average result for two or three days rather than that for a single day; a dosage determined from the analysis of many specimens of urine will almost invariably yield good results. One must not forget that the specimen of urine on arising may contain sugar but that a specimen half an hour later, which represents the quality of urine which the kidneys are secreting at the moment, may be sugar free, and the same holds true for other periods in the day. In other words the two-period test of the urine is of great value, particularly if blood-sugar determinations, especially those on capillary blood, are not available. In general the patient is actually doing better than he or the doctor thinks. On the other hand, some patients get on so well with the protamine insulin that, trusting in it, they become neglectful of diet and then show exceptionally high percentages of glycosuria, percentages which we seldom encountered years ago. With hospitalization such cases come under prompt control.

Protamine insulin can be used at the time of operations or during the course of infections. Usually it is desirable to give a maintenance dose, perhaps the same as the patient has usually employed, and then supplement it with regular insulin by a fraction-like prescription, which is based on the color reaction to the Benedict test: for example, if the maximum allowable dose of insulin were 16 units, the doses to be given with varying reactions would be:

red	orange	yellow	green	blue
16	12	8	4	0

FREE INSULIN

Diabetic patients need insulin but few need to have it given to them. Patients appreciate what they pay for. It is difficult to treat diabetic patients when or where everything is given away. Certainly patients who are in want should have insulin given to them and should not be forced to become paupers to get it, but the number of such is extremely small. I sympathize with the community which will not give insulin to the patient who has an automobile and a telephone. Furthermore, the quantity of insulin which must be given a patient to supply the daily need is not high. The cost of insulin for the average patient is less than ten cents a day.

THE ATTACK ON DIABETES

The attack on diabetes in Massachusetts first of all should center in the larger cities and around their hospitals.

In 1936 the total deaths from diabetes in Massachusetts numbered 1388.[9] Six hundred and thirty-eight occurred in cities with over 100,000 inhabitants, 318 in those between 25,000 and 100,000, and 211 in those between 10,000 and 25,000, while 97 were in cities of 2500 to 10,000, and 124 in rural districts.

In 1937, deaths from diabetes of Boston residents numbered 273, 18.3 per cent of the diabetic deaths of residents in the State.[9] If we take the Metropolitan area, the number of deaths was 607, making 40.6 per cent of the total diabetic deaths. If there are 18,000 to 20,000 known diabetic patients now living in Massachusetts or approximately 5 per 1000 and if the distribution is by population, there would be between 8000 and 9000 diabetic patients living in our Metropolitan area. Therefore, it is perfectly plain that intensive teaching can be carried out most inexpensively and efficiently in and around Boston. Expense is much less of a factor in the discovery of a case of diabetes than it has been shown to be in the discovery of new cases of tuberculosis. To learn of a new case of diabetes requires little more than the analyses of the urines of the relatives of diabetic patients, of individuals above weight and of all above the age of forty-five, particularly women and Jews. To learn of a case of tuberculosis in a child in New York State entails an expenditure of $4,418, but in those over forty-five years old only $77.[10] If we desire to spend money efficiently and economically in order to discover new cases of diabetes and to improve diabetic standards in Massachusetts, we must concentrate in and around Boston because propaganda for the purpose would be easier. We should next consider centering work in other sections of the State. Thus, Fall River and New Bedford together would make a suitable center. Lynn, Salem and Beverly might form another, as would Lowell, Haverhill and Lawrence; Worcester, Springfield and Pittsfield, each with their surrounding neighborhoods, are other likely centers.

I believe in the instruction of diabetic patients but far more in the education of the doctors who treat them. All of us doctors need more education regarding the care of diabetic patients, and I think the method which a group of us in a dozen of the Boston hospitals has adopted for the last three years is efficacious. Meeting once a year at an early dinner each one has taken part in the discussion from the point of view of the problems in his own hospital. This was furthered originally by the investigation of Dr. George W. Lynch[11] of the 301 deaths among diabetic patients in Boston during 1935. Incidentally, but 3.4 per cent of these deaths were in persons under forty years of age, and no patient died that year under the age of nineteen. I think at first we were inclined to blame the physicians without hospital connections for many of the deaths, but on critical analysis of our own work we soon found out that there was much housecleaning for ourselves to do. Therefore, first of all we focused our attention on the improvement of treatment in our own institutions. As a stimulus for this purpose Dr. Lynch selected 30 case histories of patients receiving the worst treatment and, without indicating their source, passed them around the table and we discussed them individually. I wish you could have been present the next year when we met, and still a year later, and observed for yourselves the good results of these frank discussions. I recommend this method of education, which we have found so advantageous for ourselves, be tried in other cities and in other areas. Educate the doctors who have the most patients under their care and the information will spread.

The mere talking about diabetes does good and I believe that any physician having diabetic patients in a hospital should do everything pos-

sible to show the good and bad results to those other doctors who are interested to see them. It was a pleasure the other day at the hospital to have a doctor from New Zealand, one from South Africa, one from Norway and one from Switzerland make the visit together, but the most pleasurable day in the whole year was when some fifty or sixty members of the American College of Physicians spent from 9:00 a. m. to 5:45 p. m. at the New England Deaconess Hospital in order to learn for themselves what was being done there for diabetic patients.

Each doctor of a diabetic patient and each patient should select a hospital where each will feel at home, the doctor at liberty either to care for his patient or to watch the intimate care which his patient receives and the patient to feel that he will be assured of expert attention in case of emergencies such as diabetic coma or gangrene. These latter usually are not amenable to treatment in the home — diabetic coma because of the lack of laboratory facilities and diabetic gangrene because of the drain of the many visits on the doctor's time and purse. Few of these patients, even though able and willing to pay the doctor for a week or two, can afford to do so for the time necessary to attain successful results in cases with gangrene.

The diabetic patient requires education, it is true, but in my opinion this should be given by the doctor, or a nurse under his supervision, often in association with a hospital. I think this preferable to the establishment of multiple diabetic associations akin to those which have grown up around tuberculosis. There is no gainsaying the necessity for education of the diabetic patient, because my experience with diabetic doctors under sixty years of age proves it. They show a mortality far less than that of all my patients. Since 1923, I know of no diabetic doctor among the 415 I have seen who has died of coma. Sometimes I feel that if more doctors had diabetes the treatment of the disease would advance far more rapidly.

The reasons for our failures today are becoming plainer. What a terror coma was when we failed to understand why it appeared! Now we know its causes, we can detect its approach, and slowly but surely we are learning how to explain why the treatment we once applied failed to work; thus with confidence we look forward to each new combat with a coma case.

How would you feel if a diabetic child were brought to you, known to have been treated for two years with a quack preparation, unconscious, without an examination of urine or blood since the onset of premonitory symptoms of coma four days before, nearly pulseless, so nearly moribund that she survived only forty minutes after admission to the hospital? Yet that occurred in Massachusetts this year. This case constitutes the third death of diabetic coma, since insulin was discovered, among patients under seventeen years of age while under my care — this time only for forty minutes. Graphic and startling enough were the examples of coma which came under my notice prior to 1922, some of which I recounted in that Shattuck Lecture, but I feel obliged to cite this one case seen in 1938.

What do you think will be the attitude of the medical examiner toward such a case ten years from now? What should be the reaction of the Massachusetts Medical Society, let us say in 1940, toward such treatment by one of its fellows? What was my attitude? That is easily answered. The two physicians in question were invited to see my cases at the hospital, and when they did not come, the invitation was repeated verbally and accepted. As a result, I feel sure that such a calamity will never again occur in the practice of these two doctors. Diabetic coma can be stopped, and the Massachusetts Medical Society and the State will bring this about soon. I do not believe that a death certificate with diabetic coma as a cause should be accepted without an accompanying statement of the reasons therefor — any more than a death from diphtheria, smallpox or typhoid should be allowed to pass without scrutiny.

THE RESPONSIBILITY OF HOSPITALS TO DIABETIC PATIENTS

If hospitals wish to have diabetic patients sent to them, then they should so arrange their hospital system as to give such patients good care. This implies that the hospitals will have laboratories available day and night, Sundays and holidays, and that they will have diabetic clinical charts so constructed that the staff can see at a glance summaries of examinations of urine and blood on the same side of the same sheet, together with the composition of the diet and the amount of insulin administered. Furthermore, such hospitals should have at least one nurse who not only is skilled in the care of diabetic patients, medically and surgically, but is able to share the responsibility of educating the patients in what they are to do when they go home. She should be the nurse whose duty it is to instruct all the other nurses in diabetes. Furthermore, a nurse should be available in all areas of Massachusetts so that if a doctor wishes to call on her for teaching patients in their homes or in his office, whether rich or poor, for a fee or none, she can do so.

The number of nurses necessary for this purpose in this State would be less rather than more than fifteen.

DIABETES A DISEASE FOR THE FAMILY DOCTOR

Diabetes is a disease for the general practitioner to treat. It is chronic, is susceptible to control rather than to cure, and lasts a long time. On the average the patients will live longer than their doctors will continue to practice. Moreover, treatment is now easier, due to simplification of the diet and the introduction of protamine insulin in its various forms. And there are other features which make it attractive to the medical attendant: success or failure is readily recognized; and the study or actual treatment of the disease broadens the point of view of the one who is responsible for controlling it, because the ramifications of its complications embrace all those of childhood and adult life extending into the zones of pediatrics, obstetrics, surgery, neurology and the various branches of medicine concerned with the ears, nose, throat, eyes and skin.

For years my practice was devoted to general medicine. In the course of time more and more diabetic patients have come under my care, but I have endeavored to maintain the attitude of a general medical practitioner toward my work, although now it is carried on with a background concerned chiefly with diabetes. To my great gratification, the field of the work has widened and the scope has enlarged. I know of no other disease in which it is possible to combine so many elements of medicine and surgery, held together with the links of the disease.

DIABETES AND GENERAL MEDICINE

I deprecate any attempt to treat diabetes as an entity apart from association with general medicine. Each visit of a diabetic patient constitutes a health examination, and the time spent on the diabetes per se is but a fraction of the visit. Who would want to treat such a patient with diet, exercise and insulin and forego the routine physical examination which, wholly unexpectedly, might disclose a cancer of the breast? Twice in the last three weeks such a contingency has arisen in patients without symptoms or appearance as a whole suggesting such a possibility; they were doing well and returned merely to have their diabetes "checked." Diabetic patients should be safer than the non-diabetic individual so far as cancer is concerned because of their routine health examinations. At present 10.6 per cent of my diabetic patients succumb to cancer. Just as a family doctor knows the members of his families and strives to guide their tendencies aright or to thwart them, I consider my patients as a big family unit. Ten per cent will die of cancer, 5 per cent of tuberculosis, and the incidence of the latter will be greatest in children with diabetes of long duration and in cases recovered from coma. The care of the skin must be scrupulous, and I am proud to say it is almost unknown for a patient ever to return with dirty feet, because he knows his feet will be inspected. As for the more than half who will surely succumb to arteriosclerosis, what a field for warning care!

THE CHANGING NATURE OF DIABETIC TREATMENT

If there is one thing true above all else in the treatment of diabetes it is that the treatment is not static. It differs from year to year and perhaps from month to month. A recent advance, and the one which I believe eventually will affect the situation in Massachusetts most of all, is the production of the disease experimentally, without direct interference with the pancreas, by the injection of anterior-pituitary extract. This was accomplished by Young,[12] working in Sir Henry Dale's laboratory in London, and has been confirmed by Campbell and Best,[13] of Toronto. Certainly if one can produce permanent diabetes by the injection of a hormone, there must be some counterhormone or some counterprinciple in the body which prevents all of us from having the disease. Von Mering and Minkowski[14] took out the pancreas in 1889, but we waited thirty-three years before insulin was discovered. Science today moves far more rapidly. I venture the prediction that five years will see a marked change in the type of our treatment of diabetes as a direct result of the experimental production of the disease by the injection of pituitary extract.

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Discussion

Dr. Bernard Rabinovitz, Springfield: My discussion will be limited to the diabetic situation in Springfield.

Under the influence of Dr. Joslin's ideas, we organized a diabetic clinic at the Springfield Hospital about nine years ago. There we stress the prophylaxis of diabetes by emphasizing to members of diabetic families the dangers of obesity and overeating. We also discourage marriages between individuals with a diabetic family history. Prevention of complications is urged through cleanliness and through moderation in activities such as eating, drinking and emotional stimulation.

We encourage physical exercise, wisely regulated, and wholesome hobbies. Doctors, nurses and relatives of patients are invited to attend our clinics. The care of the feet is one of the most important functions of the clinic. In older patients with diabetes, the feet are examined every six months for evidence of impaired circulation. If this condition is revealed, the patient is taught to perform special exercises and is shown other methods of physical therapy necessary to increase collateral circulation.

We teach the patient the causes and signs of protamine-insulin and insulin reactions, acidosis and coma, and instruct him as to what to do in case they occur. An elementary knowledge of food values, the physiologic requirements of the diet, the relative proportions of its essential elements and the substitution of one form of food for another are also supplied to patients and those who care for them.

Diets are made as simple as possible and scales are not used unless the patient has already become accustomed to them: we prefer wooden blocks and cardboard models. Simple household units of measurement are employed in place of the metric system. When the dietary management is kept simple the patient is more likely to adhere to the diet prescribed.

For the last nine years we have used for most patients, a high-carbohydrate, low-fat diet, averaging between 200 and 300 gm. of carbohydrate, which approximates a normal, inexpensive, everyday diet. The caloric value is kept low so as to maintain the patient's weight at slightly below normal.

We have very little trouble in using protamine insulin, and believe it to be of great advantage, especially for adult and stable patients. For some juvenile and unstable patients we add small doses of regular insulin, especially during menstruation, colds and minor infections, or where activity is restricted. We have had a few cases in which it was necessary to revert entirely to regular insulin.

Coma is a rarity among our diabetic patients. We had only 1 case in 1936, 1 in 1937. In May of this year a boy was brought to the hospital after having been in profound diabetic coma for sixteen hours. On entrance he had a blood sugar of 857 mg. per cent. Over 600 units of protamine insulin and regular insulin were required to bring him out of the coma. All three of these patients survived.

The diabetic death rate in Springfield is lower than that of New England and of the nation at large, according to the *Spectator*, an insurance periodical, and to Dr. F. Hoffman of the Biochemical Research Foundation of the Franklin Institute in Philadelphia. The surgical mortality of diabetic patients at the Springfield Hospital during the last two years was 5 per cent. We believe that the low mortality in coma and in surgical diabetes accounts for our low diabetic mortality.

In conclusion, I express my sincere gratitude to Dr. Joslin and his associates for their kind assistance, cooperation and constructive criticism, which have always been given when requested.

Dr. William Mason, Boston: My only contribution to this discussion is to emphasize one of the changing aspects of diabetes, which has already been stressed and is familiar to us all. I can best do this by stating that a series of 385 hospital admissions during a period of ten years showed the following. Admissions where arteriosclerosis was the most important complication numbered 161, with 12 deaths; those where acidosis was the most influential factor numbered 62, with 6 deaths; and those where diabetes was incidental and presented no immediate problem other than its care numbered 162, with 27 deaths. Among the latter, almost all the deaths occurred after operation.

It seems reasonable to exclude from this series the case of a girl of seven who entered the hospital in the first year of the ten-year period and died at the age of seventeen. This patient presented a typical case of undevelopment of the pituitary gland, menstruating at about sixteen, and finally died of a carbuncle and staphylococcal septicemia, with multiple abscesses over the entire body. She was admitted to the hospital in acidosis thirty-seven times, and this obviously elevates our acidosis total unduly.

With this omission, the corrected figures are 348 admissions, 161 being due chiefly to arteriosclerosis, with 12 deaths, 26 to acidosis, with 6 deaths, — including the death in the omitted case just mentioned, — and 162 to incidental diabetes, with 27 deaths. Now, in the entire ten years the ratio of admissions of those with arteriosclerosis to those with acidosis is 6:1. Taking the last five years of the period, the ratio is 12:1. Furthermore, in the city of Fall River in 1937 there were 50 deaths among diabetic patients; 40 of these were due to cardiovascular or renal disease, gangrene, coronary thrombosis, and so forth; the remaining 10 were due to miscellaneous causes; not one of the 50 was recorded as caused by diabetic coma.

This means that the most difficult problem today is that of planning for the future in a case of diabetes and not simply keeping the patient alive. A possible drawback to the use of insulin is that it has tended to make the patient careless. He soon comes to feel well, and finally ceases to see the need of doing more than to eat what appeals to him and to take just enough insulin to prevent coma. This sort of regimen fails to look to the future and to the prevention of arteriosclerotic complications. In the first place, it seems to me, the burden rests on the doctor to do all he can to emphasize that eating whatever one wants and merely taking insulin are not sufficient. Our greatest obstacle, however, is simply that of human nature. I find — and I hope I am not alone — that the hardest thing in the world is to keep a patient faithful to a regimen that will pay no dividends for twelve or fifteen years. Patients all want quick returns, they soon become careless, and some way must be devised to convince them that it is worth while to take care now, in order to prevent the later occurrence of complications which at present are causing most of the deaths from diabetes.

ATTITUDES IN RELATION TO ILLNESS

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IN PRESENTING a paper on such a general topic as attitudes in relation to illness, it is well, even though it may be self-evident, to explain how the terms of the title are being used. "Illness" is expressly chosen so as to include all forms of disturbance of function: whether it is due to disease processes; or whether, so far as can be determined by every proved method of examination, no actual physical alteration, either temporary or permanent, can be determined; or whether there is some physical change but not marked enough to account for the extent of the disability. "Attitude" refers to the point of view, the mental stage setting, the patterns or habits of thought and feeling which have become grouped together and determine the ways in which presenting situations are met and dealt with. The term is not limited to any one attitude or to that possessed by any one of the human factors in the situation, but includes that of the patient, his family and sometimes even his friends, and, most of all, the doctor. Adequate realization of the great importance of this single though fairly inclusive factor may often result in improving and even completely changing conditions in an illness that is defying all other efforts at treatment.

First of all, what is the human being's attitude in general toward the possibility or the actual presence of illness? And this includes doctors as well as laymen. Relatively few welcome the thought of being incapacitated. The malingerer, true enough, attempts to simulate disease, but he is not suffering the actual pains of the disease he simulates. The chronic neurotic may seem to be enjoying poor health, but it is not a very satisfactory form of enjoyment—just a lesser degree of suffering than the conditions from which he may be trying to escape. So it is safe to say that, by and large, men and women rightly look on illness as something undesirable, something to be avoided and generally to be feared. Illness is considered abnormal. Let us stop a moment and consider what we mean by normal. We have arbitrarily assigned to that vague term "normality" the attributes of comfort and good order, and therefore consider anything uncomfortable or disorderly as abnormal. From this point of view, of necessity, illness with its pain and disorder is abnormal. But why is not illness actually as normal as is health? From the broad aspect of the laws of nature, it is quite as normal for the tubercle bacillus to flourish as it is for storms to rage. Given certain conditions of exposure, lowered resistance or bacterial invasion, it is certainly a logical and normal result to have illness; and it is equally logical to have illness under certain conditions of disappointment, conflict and frustration. It does not follow that, because a thing is normal, it should be countenanced and nothing be done about it. But if illness and its resultant disturbances can be regarded as entirely within the realm of normal cause and effect, a better and more useful attitude is obtained. Preventive medicine recognizes this and attempts to understand and offset the normal course of influences that leads to the limitations and incapacities of disease.

The fight against disease need not lessen from regarding it as normal; rather, the campaign is more effectively organized because of the recognition of normal cause and effect. Understanding breeds confidence, and confidence lessens fear. We tend to fear what we regard as abnormal, and, conversely, to approach with more confidence what is considered normal. Therefore, if the attitude toward illness can include the realization that illness is the normal result of normal causes, a far better situation is obtained for treatment. It may be difficult, and often impossible, to establish such an attitude in a sick person, but in the doctor, because of his training and ability to take the broader point of view, it should not be impossible. The reason why such an attitude is helpful is because it makes for acceptance. This term does not mean passive resignation, but rather a dynamic state of mind which recognizes things as they are, together with the determination to find remedial measures. This reduces the extent of fear and its offshoots, anxiety and worry, and automatically results in a mental background which is favorable for recovery. The fearful, non-accepting attitude toward illness, which is by far the commonest one, is, then, the worst, and when it can be replaced by a broader, more confident acceptance, the physical and spiritual resources are freer to bring up their reserves.

One barrier in the way of obtaining this de-

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sirable attitude is the mental trick of *identification;* that is, picturing oneself in the position of some illness which one has heard or read about or perhaps witnessed. A dominant and therefore influential parent is frequently the object of identification. Many children, especially those with oversolicitous parents, are surprisingly fearful of sickness; surprising if it is not sufficiently realized how much they register from overhearing the organ recitals of their elders, with many accounts of illness and death. With pictures of suffering in their minds and little breadth of modifying experience, they naturally interpret their symptoms in extreme terms. There are many adults who have not grown up in this respect. From wider experience and unrestrained suggestibility, the first sign of malfunction means some dreaded disease. The identification may not infrequently be so complete that it is extremely difficult to tell whether actual physical disease exists. Did not all of us, in our medical school days, suffer at some time from the morbus medicorum — the conviction, if only for a few hours, that we were suffering from some disease which was being intensively studied? And even now, how many of us have had each latest test tried out, just in case . . . ! It is said that in a large hospital that boasted one of the first electrocardiographs in this country, nearly every member of the staff turned up surreptitiously to have the mysteries of his heart beat examined. If medical knowledge is not always sufficient to offset suggestibility and prevent identification, how much more natural is it that those without such knowledge should imagine themselves to be in some serious condition? It is far from a new discovery that mental states can produce the symptoms of many different diseases, and in some instances seem to be the primary cause of certain pathologic disorders. But the motivating factors and the ways by which the disturbances are effected are constantly being better understood, and are therefore subject to better treatment. Watchfulness for this mechanism of identification may enable one to produce a far more helpful state of mind in the sick person, and occasionally may actually prevent an illness; failure to recognize it has encouraged more than one long-drawn-out battle.

A second undesirable but common mental trick is what is technically known as "projection," of which one of the familiar forms is "passing the buck." By this device we try to defend ourselves from blame by externalizing, so to speak, the cause for failure: We hit the car ahead because the driver put on his brakes too suddenly, not because we were driving too close; the finished product is not so good as it should be because the tools were poor; the good or bad opinion which we consider others have of us is apt to be unconsciously the opinion we hold of ourselves. This trick is closely allied to what has come to be called "rationalization," though "false reasoning" would be a better term. Here we find the explanations for our actions or beliefs in favorable terms, whereas the actual, true explanation is not always complimentary. It has been well called "mental camouflage." The adult, as well as the small child, can escape some unpleasant task by having a pain in his stomach or head; the pleas of lack of experience can excuse one from a responsibility feared but legitimately his. It is easy to see how these three types of mental gymnastics can interfere with patterns that favor vigorous and healthy living; they all produce the habit of evading facts, of trying to make things more to one's liking, rather than help one adjust successfully to things as they are. This being so, obviously they tend to obstruct efforts which are aimed at alleviating suffering, and constitute no small part of the difficulties confronting the physician.

Another of the many barriers to a desirable attitude will be mentioned, and this one because it is so unwillingly recognized by its possessor and because of its far-reaching handicapping effect, namely *self-pity*. Though it is generally accepted as undesirable, it is perhaps not immediately evident that it is a serious obstruction. Being sorry for oneself means that one is convinced that there is a grievance, one feels justified in his position, and anyone who does not agree is regarded as unsympathetic and unkind. So long as this state of mind exists, just so long is resistance set up to efforts in the right direction. It plays into the hands of self-centered thinking and feeling, and obstructs the more wholesome factors that make for recovery and health. In the ingenuous, it is easy to recognize; but in the more complicated personality it is sometimes well and plausibly disguised. In any case, it is essential that it be dispelled. The method of eradication depends on the type of individual. With some, a direct and frank assault is best; in others, indirection, allowing self-discovery, is more effective.

It may seem unnecessary to comment on the part that the patient's family plays, because the general practitioner is in the most favorable position to see the whole picture and to be able to evaluate the influence of the various members of the family group and the effect of their attitudes on the sick person. Who has not seen an oversolicitous mother or a high-tempered father produce emotional sabotage in the children, or a dominating, paternalistic parent hamper normal, free,

adult development? But the question arises, Just how much can the family doctor do about it? There are some situations where, apparently, one might as well make no effort to change things, as defeat seems certain. However, cautious, tactful attempts may open up unsuspected possibilities, and some effort should be made to enlighten the persons involved, if not by the family doctor perhaps by another not so close. And it is apt to be the doctor's responsibility to take action because he is supposed to relieve suffering; therefore, it is up to him, when he is reasonably sure that the primary cause of the disturbance rests somewhere in the family attitude, to initiate some therapeutic attempt. He may lose a few patients, as some people do not like to be told and refuse to believe that they are the cause of trouble. But in the long run he will have a stronger and more successful position if he follows his objective knowledge and conscience.

The primary concern of this paper, however, is not so much the attitude of the patient or his family as the attitude of the doctor himself, and there are certain features of this aspect that merit some thought. It would seem that medical patterns of approach fall under two general headings: first, the ***therapeutic attitude,*** and second, the ***research attitude.*** The latter primarily regards human beings as specimens presenting interesting and intriguing problems. There is no intent to belittle this pattern because it is just as important as the other and without it there could be little if any advance in knowledge. But from the point of view of immediate care, treatment and management, this attitude lacks the friendly touch of interest in the patient as a personality, with the result that a complicated situation can be made worse. The tendency is to be consumingly interested in one type of some disturbed phenomenon or one aspect of a certain type and, for the duration of that interest, give all others little consideration. The attitude is too impersonal, too detached to give as much help or the kind of help that is needed. For instance, the study of cancer is certainly of enormous importance, but its pursuit does not require the young doctor to present and discuss a long questionnaire with a patient who is beginning a fever from some unknown and therefore frightening cause three days after her second breast amputation. This type of inconsiderate investigative enthusiasm is directly responsible for considerable unnecessary suffering. Just about every person, especially the sick person, desires to be treated as a human being and not as a laboratory specimen, and he is justified in this desire. Where the research attitude is largely tempered by therapeutic considerations we have a more satisfactory situation, possibly the ideal one. That man is fortunate indeed who is skilled in the art of treatment, and at the same time so alert in observation and ingenious in the application of his knowledge that he is able to advance and perfect the science of medicine.

The majority of men in the profession, essentially motivated by the desire to treat the sick, possess more the therapeutic attitude. For this to be most effective it needs some of that quality which characterizes the research attitude, namely ***objectivity.*** This quality allows the intellectual faculty, with all the impetus of its training and ability, to function free of obstructive emotions. When it is lacking, we find exaggerated sympathy which may be a source of comfort to some patients for a time, on the basis that misery loves company; but as judgment is thereby overinfluenced by emotion, it becomes clouded and ineffective. Objectivity does not mean the undesirable degree of impersonality already referred to, but simply the ability to stay outside of the upset feelings of the patient so as to evaluate the conditions underlying the disturbance. Emotion is contagious, — be it enthusiasm, anger or fear, — and acute situations are often more easily handled than persistent emotional states. It is only by maintaining the detachment of objectivity that our capacities for critical reasoning can do their work effectively. Furthermore, this quality includes the capacity of offsetting one's own tendency to suggestibility. It helps, in judging the patient's responses to his illness, to detect, from knowledge of the kind of person he is, whether he is over-reacting and exaggerating the severity of the symptoms or whether he is courageously suppressing his suffering. It should help more than it does to prevent the indiscriminate acceptance of every new and enthusiastically presented medicine or system of treatment.

There is one item in the therapeutic attitude that still needs some attention drawn to it, in spite of the fact that much has been said and written about it in recent years, and that is the tendency to discount the importance of psychological factors in illness. The principal emphasis has long been too much on physical aspects, the reaction of the body tissues to altered chemistry or invading organisms, so that not enough attention has been paid to the mental reactions of the patient toward his illness or the extent to which mental activities affect health. In general, there is not sufficient understanding of those mental illnesses commonly called the neuroses, psychoneuroses, functional nervous disorders, "nerves,"

which are usually the result of emotional mismanagement, whether or not actual physical disease is present.

The view is held, or its opposite only begrudgingly admitted, by too many that mental illness means insanity and that emotional mismanagement with its disturbed mental and physical function is always due to underlying physical abnormality or else merely perverse character traits. The opposite view, that mental disorders are always of psychological origin, is equally untenable. There is some truth in each contention but neither is entirely true, so that there are obvious hazards to both physician and patient, but more particularly the latter, when either view is exclusively maintained. The former is the more important because it is more widespread. The best medical schools are giving more adequate instruction along these lines, but the majority of practicing physicians now in full flight have had to learn from their own experience how far-reaching is the effect of mental attitudes on bodily conditions.

The experience of recommending operation and seeing a normal appendix removed from the normal abdomen of a young girl unable to continue school because of supposed repeated attacks of pain, will make the honest physician wonder why he did not place more importance on the facts that this girl had left several schools, was not doing well in her studies, and had a more successful older sister who was favored by her parents. The experience of unsuccessfully treating a middle-aged man by diets and powders for "indigestion" of several months' standing, only to see the condition cleared up by mental treatment, will cause the open-minded physician to go more carefully into the emotional background and history, in order to find out if there is not some important conflict behind the disturbed function.

Examples of this sort could be continued indefinitely, drawn not only from the experience of psychiatric practice but also from the experience of consultants in general medicine. At least three such consultants who are much in demand say that the percentage of nervous disorders among the patients referred to them for diagnosis of supposed physical disease is so high that they are beginning to consider themselves as psychiatrists. The question submitted to six successful, active, general medical practitioners as to what percentage of primarily nervous malfunction appeared in their practice, showed an estimate of from 30 to 75 per cent, with an average of 60 per cent. Obviously some men see more of this type of case than others, for the type of practice varies as well as the type of physician. But many will fail to recognize its presence. Why is this so? Lack of experience or perception is not the only cause. A very potent and possibly the most important explanation can be found in the closed mind, in the attitude based on prejudice against the fact of psychogenic illness, regarding such as a stigma of peculiarity or weakness. Unfortunately, this attitude is not confined to the lay mind. It is more understandable there; but it is impossible to condone it in the medical mind, which, with its scientific traditions, should be better able to cultivate and maintain an unbiased point of view in etiologic considerations. A prejudiced attitude does not have to stay prejudiced, except of course some of our little pet ones! But certainly not in the field of medicine, for here, as in every science, new discoveries broaden the horizon and necessitate the ability to change and enlarge previous conceptions. For patients whose illness is primarily mental, this prejudice is often one of the most difficult hurdles on the road to recovery. It is hard enough if only the patient possesses it; it is still harder if the family and friends are of that opinion; but it is hardest of all if the doctor feels the same way, because his is a position of great influence.

Attitudes need not remain rigid and fixed—they should have an inherent stability, enabling them to meet new conditions and to change their direction but still maintain a consistent balance. It is the physician's business to search for the cause of illness and apply the best knowledge he has in treatment. In this search, it is incumbent upon him not only to auscultate and percuss but also to look for the less tangible causes of illness; and, where it is indicated, the treatment does not rest with pills and tinctures but includes a large measure of educating the attitudes of all concerned.

Valleyhead, Concord.

Discussion

Dr. Arlie V. Bock, Cambridge: The importance of the point of view brought forward by Dr. Lunt cannot be overstressed in the general practice of medicine. We are too much accustomed, it seems to me, to treat symptoms and not to look at the patient as a whole.

It may be worth while to consider from this general point of view a few of the problems that are presented to all of us every day by our patients. We may assume that everyone we know is in trouble of one sort or another. Such difficulties are not always apparent from the particular symptom that the patient presents, and have to be dug after a bit in order for us to get the correct picture. The common attitude, it seems to me, on the part of too many physicians is to accept at face value the condition about which the patient first complains. This is in many cases a mistake, since the underlying circumstances remain unknown.

A fact that Dr. Lunt stressed somewhat will bear repetition. The great majority of the patients with whom

we deal do not have any formal mental illness. They have no neurosis. They are not neurasthenic patients. They do not have psychopathic personalities, and they are not suffering from major psychoses. But they are suffering from attitudes toward their conditions of life which are expressed in terms of various, often seemingly minor complaints which lead them to consult a physician.

One example is the problem of constipation and autointoxication. It is remarkable how many patients one sees who have been to numerous physicians and been told that they are suffering from autointoxication. If there is such a thing as autointoxication arising from constipation, I have seen no proof of it in the twenty-three years since I left medical school; yet the persistence of this belief on the part of patients in general and of very many physicians is contributing to personality damage, I believe, in the particular patients that we see.

Another mistaken attitude of ours has reference to hypertension. How many patients do we see who have been told that Dr. So-and-So found their blood pressure to be 190 and two weeks later had reduced it to 180 or perhaps 185? We should instead take the position that we have no specific means of reducing blood pressure; and, what seems to me much more important, we should encourage a patient to adapt himself to this condition by easing his load wherever possible. It is a mistake to give him the notion that we can reduce blood pressure by any drugs that we now have at our command.

Another complaint that bothers many patients is "gas in the stomach." How many prescriptions have doctors given for this complaint. Gas in the stomach is due occasionally to ulcers, gall stones or other pathologic conditions, but in most cases this condition arises because the subject is disturbed about something; and when it recurs day after day, week after week and month after month, it may be assumed that something is wrong with the patient's reaction to life. We must investigate in order to see whether we are dealing with organic disease; failing to find it, we are not thereby justified in prescribing bicarbonate of soda, pepsin and the like. The same principle, as mentioned by Dr. Lunt, applies to patients who come to us complaining of repeated attacks of indigestion. If we know that such attacks are not associated with ulcers or gallstones, we should suspect that the patient is suffering from some other condition, some abnormal reaction to his family, business or associates. Until we get to the bottom of this condition, we cannot very well eliminate the indigestion.

Still another common complaint is sinusitis. Now, there are many cases of chronic sinusitis that are the consequence of surgical interference in the nose, but most cases are a fence, a mechanism to fend off certain obligations.

These are only a few of the simple complaints brought up in everyday practice which have a greater significance than the patient realizes.

DR. G. COLKET CANER, Boston: It has been very worth while to have the importance of attitudes emphasized as Dr. Lunt has done in this interesting way. We physicians are trained to think in terms of symptoms, pathology, diagnosis and prognosis. It is important also to train oneself to think in terms of attitudes. The physician inevitably develops a very objective attitude toward illness. This attitude arises from his familiarity with illness, and may be helpful in certain ways. It helps him to think clearly and to have good judgment, and it is helpful also to the patient because he necessarily absorbs some of the physician's objectivity. However, most patients have a very subjective and fearful attitude toward illness. They are preoccupied by what the symptoms mean for them, and fear the worst. It is easy for the physician to forget this, thinking in his own objective way, and it is easy for him to say things which precipitate marked fear in the patient's mind. I suppose that almost every physician has seen numerous patients who have developed psychoneurotic symptoms as a result of fears caused by something that another physician has said without realizing that it would upset them. In order to obviate this as much as possible, it is very important, I think, to bear the apprehensive attitude of the patient constantly in mind.

I remember the late Dr. Wyllys Taylor's saying that in many cases the symptoms are not so important as what the patient thinks they mean and his attitude toward them, and I have found it very helpful to keep this in mind. It has aided me in unearthing fears in the patient's mind which were really the cause of his symptoms and which might otherwise have been missed.

The attitude of the patient is significant no matter what his illness may be. His attitude often determines how much he will suffer, and in many cases may actually influence the course of the illness. An individual's attitude toward life, his attitude toward himself and toward others, toward success and failure, toward disappointment and frustration, determine to a large extent whether he is likely to become unduly upset as a result of the stresses and strains of life. In other words, one's attitudes tend to determine whether one is likely to develop a psychoneurosis, or even a psychosis.

In the treatment of psychoneuroses, it is essential to direct one's efforts toward modifying the attitudes which have led to the conflicts causing the symptoms. These attitudes are often more or less unconscious. Either the patient is not aware that they exist, or he does not realize that his symptoms are in any way attributable to them. It is, of course, difficult to modify attitudes. It takes time and skill. One must usually obtain some emotional response from the patient, and this may require considerable art, but if one has clearly in mind what one is seeking to accomplish, one may often secure results which are very worth while.

SULFANILAMIDE: ITS MODE OF ACTION AND USE IN THE TREATMENT OF VARIOUS INFECTIONS

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BOSTON

LAST year before the combined clinical section of this society, I[1] discussed some of the factors concerned in the prognosis of hemolytic streptococcal infection and reported the results of our experience with sulfanilamide. I now summarize the results of our recent studies concerning the mode of action of this drug in vitro, together with some observations dealing with the results of treatment in streptococcal, gonococcal, meningococcal and urinary-tract infections.

MODE OF ACTION

Ever since sulfanilamide was introduced for use in the treatment of infectious diseases, there have been numerous studies concerning the mechanism of its action in vivo and in vitro. Various organisms and different experimental animals have been used. While the information is far from complete, several suggestions have been made which merit consideration, since they are based on accurate clinical and experimental observations.

The following suggestions relative to the action of sulfanilamide have been offered: (1) it acts mainly as a bacteriostatic agent; (2) it stimulates phagocytosis; (3) it neutralizes bacterial toxins; (4) it is bactericidal under certain conditions; (5) it delays the growth of organisms until mononuclear phagocytes accumulate; (6) it alters the organisms so that phagocytosis can take place. Some of the differences of opinion are undoubtedly due to variance in the methods employed for studying its action, and there is also evidence that its action on one organism may be different from that on another.

In so far as the hemolytic streptococcus is concerned, it is now clear from our work[2] and that of others[3] that sulfanilamide exerts a definite bacteriostatic effect on the growth of this organism in vitro. This can best be demonstrated when small numbers of organisms per cubic centimeter are used and when whole blood rather than broth is employed as a culture medium. In some cases hemolytic streptococci are actually destroyed when sulfanilamide is added to whole blood, and this is especially true if the whole blood contains antibodies. That is to say, the bactericidal action of whole blood containing antibodies and sulfanilamide is greater than that of a corresponding sample of whole blood without sulfanilamide. These observations suggest that when the multiplication of small numbers of organisms is suppressed, the antibodies which are present in whole blood operate more effectively.

Various studies of the action of sulfanilamide in the body indicate that there are at least two essential conditions for therapeutic effectiveness. First, it is necessary to subject the organisms to a concentration of the chemical that will produce maximal bacteriostasis; and secondly, the body must retain or acquire the power to rid itself of the viable organisms which are producing the disease. In our own experience, maximal bacteriostasis can be accomplished by maintaining a blood concentration of from 7 to 10 mg. per cent. It is also necessary for the body to be able to phagocytize organisms and destroy them; this requires active, viable cells and specific antibody. In experimental animals the importance of specific antibody for phagocytosis seems to vary with the animal used and the strain of infecting organism. It is perhaps well to recall that even when clinical recovery occurs the local focus may not be sterilized. This is true in many hemolytic streptococcal infections whether or not they have received sulfanilamide, and Longcope[4] has amply demonstrated that the administration of the drug for from four to thirty-two days will not always eliminate hemolytic streptococci from persistent infections of the tonsils. Somewhat similar results have been obtained in puerperal infections, in mastoiditis and in experimental animals; that is, recovery from clinical infection may occur without the sterilization of the local focus of infection.

These observations, together with the fact that one may see recurrences or relapses of infection following the withdrawal of sulfanilamide, suggest that the final destruction of organisms depends on the action of the defense mechanism of the body. That is to say, unless the defense mechanism can prevent a free growth of organisms subsequent to withdrawal, an exacerbation of infection with reinvasion of the tissues will thereupon occur.

SULFANILAMIDE IN STREPTOCOCCAL INFECTIONS

At present there is not sufficient information at hand to assess the action of sulfanilamide on all

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forms of hemolytic streptococcal infections in man. Certain facts have, however, been obtained, that mark this drug as exerting the most remarkable results in some infections.

So far, sulfanilamide has been shown to be effective in man against Group A strains of hemolytic streptococci, and in animals against some but not all strains of Group C. It has been found ineffective in anaerobic streptococcal puerperal sepsis[5] and in infections of the urinary tract due to Group D streptococci.[6] I confine my discussion to cases of bacteremia, meningitis, puerperal sepsis and peritonitis. I[1] have recently summarized its effect on other forms of streptococcal infection. The above conditions have been selected for discussion because they represent the severest test of efficiency for sulfanilamide.

Bacteremia

It is now well recognized that bacteremia occurring in connection with hemolytic streptococcal infection is always of very grave significance. In 246 cases of streptococcal infection accompanied by bacteremia reported by Keefer, Ingelfinger and Spink[7] the mortality rate was 72 per cent. Longcope[4] records a mortality rate of 75 per cent in 166 cases. While there are some differences in the mortality rate in various groups of cases depending on the portal of entry, the age of the patient, the accessibility of the infections for surgical drainage, the presence of debilitating disease and other factors, the rate was high regardless of any of these factors. The patients who recovered fell into two main groups: cases with a temporary bacteremia in which there was clearing of the blood stream without the formation of focal abscesses, and cases of bacteremia with clearing of the blood stream and with focal abscesses in locations that could be drained surgically. On the other hand, the patients who died had a rapidly advancing local lesion, bacteremia and no evidence of localization, or bacteremia with or without clearing of the blood stream and with organisms localized in regions or areas that could not be attacked surgically. These various features should be recognized in studying the course of events in cases with bacteremia which are treated with sulfanilamide.

We have had the opportunity of treating 15 cases of hemolytic bacteremia with sulfanilamide, with 10 recoveries. In the patients who recovered, the local focus showed signs of regression, the blood was gradually cleared of organisms, the leukocyte count frequently increased, and the temperature was gradually reduced to normal. In some cases a local focus of suppuration appeared, so that an abscess was drained. In the fatal cases there was peritonitis or a local focus that could not be drained surgically (thrombophlebitis of jugular vein), streptococcal pneumonia complicated by pneumococcal infection, or multiple septic arthritis (Table 1).

Table 1. *Results in 15 Cases of Streptococcal Bacteremia Treated with Sulfanilamide.*

DISEASE	NO. OF CASES	RECOVERED CASES	FATAL CASES
Puerperal sepsis	3	3	0
Cellulitis	3	3	0
Multiple arthritis	2	1	1
Thrombophlebitis of jugular veins	1	0	1
Bronchopneumonia	2	0	2
Peritonitis	1	0	1
Otitis media	2	2	0
Cryptogenic sepsis	1	1	0
Totals	15	10	5

Figure 1 illustrates the course of the temperature and the bacteremia in a girl of seven who developed acute hemolytic streptococcal mastoiditis following otitis media. Subsequent to the giving of sulfanilamide and mastoidectomy the blood stream cleared rapidly, the fever subsided, and the patient made a rapid recovery. While some patients with bacteremia following mastoiditis recover after operation, our experience, together with that of others, indicates that the prognosis is always grave.

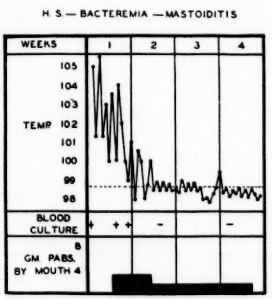

Figure 1.

Figure 2 shows the course of the temperature and bacteremia in a man of thirty who developed a cellulitis of the right arm. Following incision and drainage of the infected area and the administration of sulfanilamide, the blood was cleared of organisms, although the patient developed pericarditis and pleurisy, an abscess of the thigh and arthritis of the right elbow joint. The continued use of sulfanilamide and blood transfusions, together with surgical treatment of the local foci of infection, was followed by complete recovery. After the giving of sulfanilamide and

the clearing of the blood stream the leukocyte count increased. During recovery the specific antibody titer of the blood increased, emphasizing the importance of the specific immune response in these cases.

Meningitis

The severest test that can be demanded of a therapeutic agent is that of its effect on patients with hemolytic streptococcal meningitis. The usual mortality rate is about 98 per cent. From 1901 to 1937 there were recorded in the literature[8] 110 re-

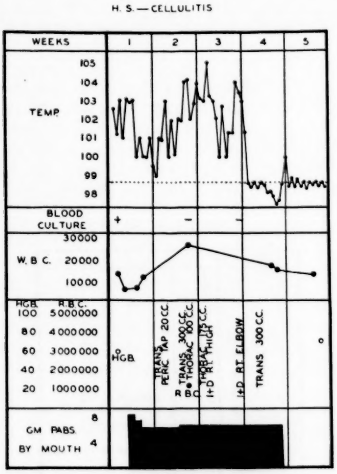

Figure 2.

coveries from hemolytic streptococcal meningitis. Since the introduction of sulfanilamide and Prontosil Soluble at least 60 cases have been treated with either or both of these drugs; in these recorded cases there were 47 recoveries. The results leave not one shred of doubt that this chemical is the most effective and potent substance developed so far for the treatment of this type of case. While it is true that most cases of meningitis have followed otitis media and mastoiditis, and that other forms of treatment besides sulfanilamide have been used, including whole blood transfusions, operations on infected mastoids and the repeated drainage of the subarachnoid space, there is no question that sulfanilamide has played an enormous part, since similar forms of treatment without it have as a rule been almost completely ineffectual. It is extremely important to realize that it is probably essential to employ many of the procedures mentioned, since recovery depends not only on the action of the drug but also on the defense mechanism of the body.

Figure 3 illustrates a case successfully treated with sulfanilamide. A young girl developed hemolytic streptococcal meningitis following a traumatic fracture of the skull.* The wound was treated surgically, the spinal fluid was drained, blood transfusions were given, and sulfanilamide was administered by mouth daily for four weeks. The spinal fluid continued to contain organisms for three weeks and the fever continued for six weeks. All the procedures listed undoubtedly contributed to the recovery, but it is unusual for anyone to recover

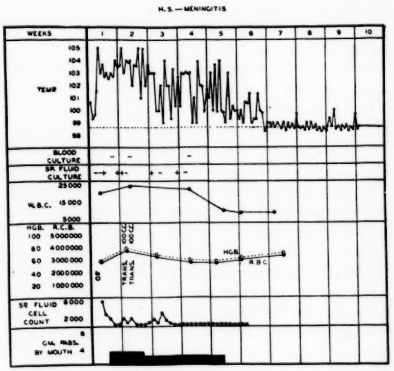

Figure 3.

from hemolytic streptococcal meningitis when sulfanilamide is not given.

Puerperal Sepsis

With the studies of Colebrook and his associates,[3] Foulis and Barr,[9] Gibberd,[10] and ourselves,[1] there no longer remains any doubt that sulfanilamide is effective in the treatment of puerperal sepsis. In the cases of local infections of the uterus the infective process is prevented from spreading, there is no blood invasion, the duration of the hospital stay is shortened, and the death rate is reduced. In the cases with bacteremia, with or without peritonitis, or extensive thrombophlebitis the results are likewise impressive, since the mortality has been reduced from 70 to 40 per cent. Colebrook and Purdie[11] have lowered the fatality rate in their cases of puerperal sepsis from 23 to 7 per cent

*I am indebted to Dr. Donald Munro of the Neurosurgical Service, Boston City Hospital, for the privilege of seeing this patient.

through the use of Prontosil Soluble and sulfanilamide. Longcope[4] recently recorded a case of puerperal sepsis with bacteremia in which recovery followed treatment with sulfanilamide. There was an early invasion of the blood, high fever and a poor leukocyte response. Following the administration of sulfanilamide there was a rapid decrease in the number of colonies of hemolytic streptococci in the circulating blood, and finally clearing of the blood stream, a fall in temperature,

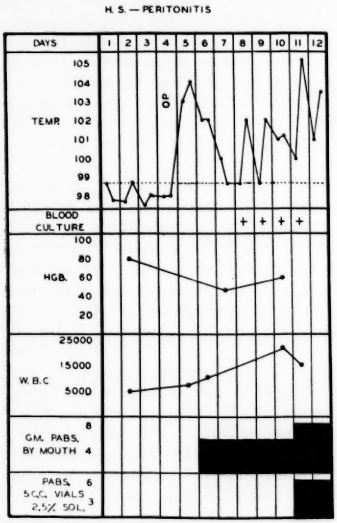

Figure 4.

an increase in leukocytes and a rapid recovery without focal metastases.

In appraising the results in these cases, it is well to recall that anaerobic streptococcal infections seem to be resistant to chemical therapy, whereas hemolytic streptococcal infections are very effectively controlled. Local infections are controlled more effectively than are those that have invaded the blood, although the results in the latter are also impressive.

Peritonitis

Cases of hemolytic streptococcal peritonitis that recover are exceedingly rare, although recoveries following sulfanilamide therapy have been reported by Colebrook and his associates[11] and by Longcope.[4] So far we have not had an opportunity to observe a patient who recovered from this disease. Figure 4 shows the course of events in a single case which was fatal. This patient had a supravaginal hysterectomy for fibroids of the uterus. Almost immediately following operation there was high fever and signs of peritonitis with bacteremia on the fourth day. In spite of large doses of sulfanilamide the blood continued to show organisms and the patient died.

SULFANILAMIDE IN GONOCOCCAL INFECTIONS

Sulfanilamide has been used with varying degrees of success in the treatment of gonococcal urethritis,[12, 13] vulvovaginitis, cervicitis and peritonitis, arthritis and ophthalmia. From our clinic Spink and Gaston[13] reported the results in 21 cases of urethritis, and Rantz and I[14] have recently summarized our results in the treatment of 14 cases of gonococcal arthritis and in a study of its action in vitro. In brief, it can be said that sulfanilamide is bacteriostatic as well as bactericidal for the gonococcus in vitro. This is most convincing when whole blood or plasma is used and the organisms are subjected to a concentration of more than 5 mg. per cent.

We[14, 15] have found that synovial fluid can be sterilized within forty-eight to seventy-two hours after the administration of the drug by mouth and that both the blood and synovial fluid become highly bactericidal. In some cases the local focus in the genitourinary tract can likewise be freed of gonococci. Therefore there are good reasons for believing that the drug would be effective in treating gonococcal infections of the joints. Our experience so far indicates that it is very effective in patients who have infected synovial fluid, in that it sterilizes the fluid, reduces the duration of the hospital stay, reduces the duration of the inflammation of the joints and aids in the sterilization of the local focus of infection. Moreover, the end results in so far as joint disability is concerned have been excellent, since all our patients have recovered completely. The cases in which the results are less striking are those with a local focus, sterile effusions into the joints and a low antibody response. It is possible, and indeed not unlikely, that some of these cases of arthritis have a somewhat different pathogenesis.

Sulfanilamide is incapable of sterilizing the local focus of infection in all cases, and for this reason one must be cautious in the interpretation of immediate clinical results. Since patients with latent infection may spread the disease, and since the combined activity of the body defenses as well as sulfanilamide are required in order to bring about sterilization of a focus of infection, other methods of treatment should not be neglected.

SULFANILAMIDE IN MENINGOCOCCAL INFECTIONS

Meningococcal meningitis has been treated by sulfanilamide with extraordinarily good results. It has been demonstrated that this drug is capable of protecting mice against fatal infective doses of meningococci when the mucin technic of Miller is used, and in the test tube it has a marked and measurable bacteriostatic effect. In the presence of adequate concentrations of sulfanilamide these organisms do not seem to reproduce themselves, and this effect is noted even in the spinal fluid of treated patients. We have been unable to grow meningococci from the spinal fluids of patients with meningitis within twenty-four to forty-eight hours

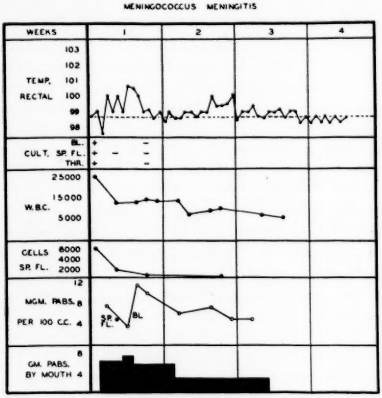

Figure 5.

after exhibition of the drug by mouth, so that there is little doubt as to its profound effect. In order to accomplish this objective the concentration of sulfanilamide in the blood and spinal fluid should be at least 10 mg. per cent. Inasmuch as the drug diffuses into the cerebrospinal fluid with great rapidity, it is unnecessary to give it intrathecally. Figure 5 illustrates the results in a case which we observed and studied. A woman of fifty-five with a diagnosis of meningococcal meningitis was admitted to the hospital on the third day of her illness. The blood culture, spinal-fluid culture and throat culture showed meningococci. There were fever, leukocytosis and an increase in the cells in the spinal fluid. Following the administration of sulfanilamide by mouth the spinal fluid was sterilized within twenty-four hours and the patient showed rapid improvement, in spite of the fact that low-grade fever of three weeks' duration was present. The blood level of sulfanilamide was kept at a level of 5 mg. per cent or higher during the period of treatment.

Preliminary reports from various clinics indicate that the fatality rate can be reduced in this disease, and there is suggestive evidence that the drug is as effective as antiserum in reducing fatality rates.

There is reason to believe that sulfanilamide may not be equally effective against all strains of meningococci, so that it may be wise to use serum and sulfanilamide in cases in which the response to sulfanilamide alone is not prompt. Certainly for the present the spinal fluid should be carefully studied for organisms at frequent intervals, and if there are no signs of a rapidly subsiding infection, serum should be used. In all cases adequate doses of sulfanilamide should be given before one decides that the drug is ineffective or that the strains are resistant.

While it would be premature to say that sulfanilamide is as effective as antiserum in the treatment of meningococcal infections, since the experience with serum treatment is much more extensive, from the present indications there are excellent grounds for believing that sulfanilamide will be effective in a high percentage of cases.

SULFANILAMIDE IN INFECTIONS OF THE URINARY TRACT

There is general agreement that urinary tract infections due to *Bacillus coli, B. proteus, Staphylococcus aureus* and *B. influenzae* are favorably influenced by sulfanilamide. Bliss and Long[6] have reported failure in infections due to Group D streptococci, and Helmholz[16] has not observed favorable results in those with *Streptococcus faecalis*. There is no doubt that sulfanilamide exerts a measurable bacteriostatic effect in urine, and in clinical cases it has been found effective even when the urine is alkaline. As one studies these infections of the urinary tract in adults, it becomes evident that the drug inhibits the growth of organisms so that in some cases there is complete sterilization of the urine. In others the organisms disappear during the administration of the drug but reappear when it is discontinued. While the drug is of distinct value in these cases, its field of greatest usefulness has not yet been determined.

Figure 6 illustrates the course of events in a single case of pyelonephritis caused by *B. coli*. A twenty-two-year-old, pregnant woman developed the disease with four episodes of fever and chills. Between attacks of fever, bacilluria was always present. At the end of the third attack she was given sulfanilamide by mouth; as a result there was a sharp decrease in the number of organisms and leukocytes in the urine, and it was impossible to grow organisms from it for several days. Following

withdrawal of the drug there was an exacerbation of the fever and a recurrence of the signs of pyelonephritis. After resumption of sulfanilamide all the symptoms disappeared; the urine became sterile, and has remained so for twenty-eight weeks. This case illustrates the fact that sulfanilamide may have a profound effect on the number of organisms in the urine and that it should be continued for a long period of time before withdrawing it. It

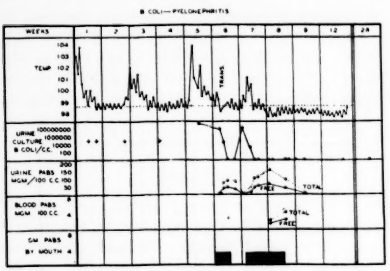

Figure 6.

also suggests that there are other factors in the recovery mechanism which are independent of the action of sulfanilamide.

TOXIC MANIFESTATIONS OF SULFANILAMIDE

While sulfanilamide has a relatively low toxicity for animals, it is now known that it produces a variety of unpleasant symptoms, and in rare cases

Table 2. *Summary of Toxic Manifestations of Sulfanilamide.*

SYMPTOM OR SIGN	TIME OF APPEARANCE	TREATMENT	OUTCOME
Cyanosis	First or second 24 hours	None, unless there is anorexia; in that event discontinue the drug.	Prompt recovery
Nausea, vomiting, giddiness, weakness.	First 24 hours or longer	None; they are usually not severe enough to necessitate discontinuance.	
Anemia	3-7 days	Stop drug immediately; force fluids to 3000 cc. daily; give transfusions.	Recovery
Agranulocytosis	14 days or later	Stop drug; give Pentnucleotide and transfusions.	Fatal in most cases
Fever	7-9 days	Discontinue drug; force fluids.	Complete recovery
Skin eruptions	7-9 days	Discontinue drug; force fluids.	Complete recovery

the response may be exceedingly alarming and indeed dangerous. It is impossible to predict what toxic features will appear in a given case. Some individuals can take 1 or 2 gm. a day for months without the slightest discomfort. In others, signs of intoxication occur within a short time. Table 2 summarizes the main toxic effects. Cyanosis, malaise, anorexia, prostration, dizziness, headache and a feeling of depression are common. These symptoms come on within the first or second twenty-four hours of the administration of sulfanilamide, and may continue as long as it is ingested. Despite the discomfort caused, they are not of sufficient significance to force one to omit the drug.

There are, however, certain toxic features, which are of distinct importance since they call for immediate cessation of sulfanilamide and the substitution of active treatment of the secondarily produced disease. These are hemolytic anemia and agranulocytosis. The febrile reactions and skin eruptions are likewise important.

Hemolytic Anemia

We have observed 1 severe case of hemolytic anemia following the use of sulfanilamide in a patient with gonococcal arthritis. The course of events is shown in Figure 7. Four days after the

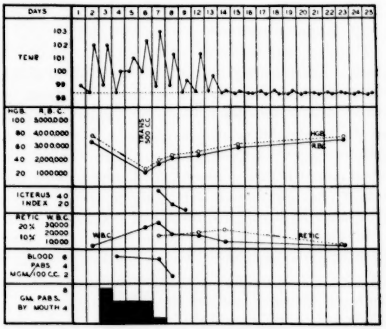

Figure 7.

commencement of sulfanilamide treatment the patient developed a severe anemia, with leukocytosis, reticulocytosis, jaundice and severe prostration. When the drug was discontinued and a blood transfusion was given, together with the forcing of fluids by mouth, there was a rapid regeneration of the blood, a prompt disappearance of the jaundice and a decrease in the leukocyte count. Following this episode the temperature returned to normal, the acute arthritis disappeared, and the patient made a complete recovery. This case was very much like all other cases of hemolytic anemia that have been recorded. It is noteworthy that the reaction developed quickly — within four days after the drug was started. Moreover, the concentration in the blood never went above 6 mg. per

cent. It is also evident that recovery took place following the forcing of fluids, cessation of the drug and transfusion. By this case, as well as by others recorded in the literature, the characteristic features of this complication are shown to be a rapidly progressive anemia coming on within three to five days after administration of the drug; polymorphonuclear leukocytosis with reticulocytosis; jaundice and signs of diminished hepatic function, in some cases; and prompt recovery following withdrawal of the drug, the use of transfusions and the forcing of fluids (3000 cc. a day).

The anemia, which is often severe, may develop with great rapidity so that the erythrocyte count and the hemoglobin decline to levels of 30 to 40 per cent of normal within three to five days after the drug has been started. A stained smear at this stage shows anisocytosis, achromia and many nucleated erythrocytes and reticulocytes. The white-cell count is usually increased, and varied in the reported cases from 20,000 to 87,000. I have been told of a case in which the count reached 125,000. There are many immature neutrophils and myelocytes; platelets are normal in number.

Jaundice was a feature of most of the recorded cases. Anemia may appear without clinical jaundice, although there may be evidence of increased blood destruction when the urobilinogen contents of the stools and urine are studied. Bilirubinuria has been noted in some cases, and there is evidence of impaired hepatic function as determined by the bromsulfalein-excretion tests. In one case of hemolytic anemia, hemoglobinuria was noted.[17]

In short, cases of acute hemolytic anemia have been observed to appear within the first five days following treatment. The treatment consists of stopping the drug, forcing the fluid intake to 3000 cc. daily and giving transfusions. Inasmuch as the anemia can develop rapidly and occur without icterus, the hemoglobin and erythrocyte count should be followed carefully during the first week of treatment.

Agranulocytosis

This is the most serious complication of sulfanilamide therapy. With a few exceptions the reported cases have ended fatally. Several interesting and important features have been brought out from a study of these cases. It is a striking fact that no case occurred before the fourteenth to the sixteenth day after the onset of treatment. In some cases the leukocyte count fell after the drug had been stopped, and in a few it decreased only when the drug had been resumed after a preliminary withdrawal. It is not, however, always clear from the reports that the decrease in the leukocyte count occurred in an abrupt manner, since the counts were not recorded daily. That it does drop abruptly in some cases there is no doubt.

In the fatal cases, death has generally occurred within two or three days after the onset of agranulocytosis. These cases serve to emphasize the importance of making repeated leukocyte counts in all individuals who have been receiving the drug for a week or longer.

Febrile Reactions and Skin Eruptions

Hageman and Blake[18] have called attention to febrile reactions with or without skin eruptions following the drug. The febrile reactions without the skin eruptions may be difficult to interpret, since they may be due to the drug itself, to an exacerbation of the infection or to the occurrence of a complication. The time relations may aid in the decision, for the drug fever occurs most often within seven to ten days after starting the drug, but may appear as early as the fourth or as late as the fourteenth day, and it may persist for as long as two to nine days, but more often two to four days. The temperature may vary from normal to 106°F., the average being 101 to 103°F. Other helpful aids in diagnosis are the presence or absence of accompanying symptoms or signs of an exacerbation of infection. For example, we have noted exacerbations of arthritis and fever coming on within a short time following the withdrawal of the drug, and a remission of symptoms following resumption. In such cases there seems to be no doubt that the fever was due to an exacerbation of the infection. In others this is very uncertain. Figure 8 shows an exacerbation of the fever within seven days after starting the drug. Although sulfanilamide was continued and there were no clinical exacerbations of the infec-

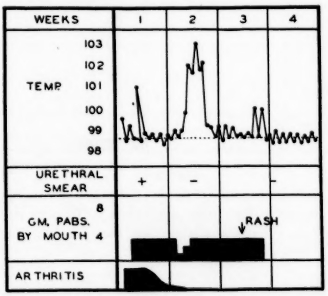

Figure 8. *Fever and skin eruption following sulfanilamide in a patient with gonococcal arthritis. Fever appeared before the rash and was self-limited in duration. The arthritis disappeared promptly and the urethral exudate was sterilized of gonococci.*

tion during this time, the temperature returned to normal while the drug was being given. This experience, together with those in other cases, has led us to believe that these febrile reactions may be self-limited in duration and may disappear in spite of the fact that the drug is continued. In some cases we have noted that the fever appeared before the rash. When the drug is discontinued the rash usually disappears promptly, but it may persist for several days.

The eruptions have varied considerably and have consisted of urticaria, exfoliative dermatitis and morbilliform, scarlatiniform and purpuric rashes. In a few cases they are precipitated by exposure to light. As related above, when the eruption has once made its appearance it may persist for some days after the withdrawal of the drug.

DOSAGE

Inasmuch as the purpose of sulfanilamide is to suppress the growth of micro-organisms, and it is known that this is accomplished only when they are subjected to an adequate concentration, it is necessary to give doses that will bring about the optimum concentration in the blood and tissues. From experiments in vitro as well as in vivo, it appears that a concentration of 7 to 10 mg. per cent in the circulating blood is necessary for the maximum effect. To accomplish this it is necessary to give moderately large amounts by mouth. We have usually given 0.066 gm. per kilogram of body weight as an initial dose, followed by 0.6 gm. every four hours. In most adults of average weight we have given 8 gm. during the first twenty-four hours. After that time we have continued the drug in daily doses of 4 gm. It may be necessary to give much larger amounts to some patients in order to reach the optimum level in the blood. This seems especially true when large amounts of fluid are being given at the same time.

The sulfanilamide of the blood is determined every day during its administration in order to be certain that the optimum level in the blood is reached. After that period, the test is repeated every forty-eight hours. Hemoglobin and leukocyte counts are done daily, and if the concentration of the blood increases above 10 mg. per cent, or if toxic symptoms such as anemia, fever and skin eruptions occur, it is discontinued and blood transfusions are given if necessary. In the face of severe streptococcal meningitis we have continued the drug even with a rapidly advancing anemia, since we found that the latter could be controlled by blood transfusions and since we had very little to gain by discontinuing it in the presence of such a highly fatal disease.

COMMENT

A summary of our experience with the mechanism by which sulfanilamide produces its results in hemolytic streptococcal infection indicates that it is bacteriostatic. When antibodies are present so that phagocytosis and destruction of organisms take place, sulfanilamide given in adequate concentration aids in the operation of the mechanism of destruction. There is also evidence that the rate of multiplication of streptococci is reduced; this enables the body to mobilize its defense mechanism and to rid itself of the viable organisms which are producing the disease. In the final analysis, experiments with animals and studies in man indicate quite clearly that the body-defense mechanism is of the highest importance in the final outcome. In all the patients we have studied in whom recovery took place following bacteremia, there was convincing evidence that antibodies for the homologous organism were present and were undoubtedly responsible to a large part for recovery. Table 3 shows the results of bactericidal tests on the blood of 2 patients who recovered from bacteremia; it is to be noted that on recovery the bloods, with or without sulfanil-

Table 3. *Bactericidal Action of Whole Blood from Patients Recovering from Streptococcal Bacteremia following Use of Sulfanilamide.*

Test Mixtures	Dilution of Organisms						
	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}*
Patient 1							
0.5 cc. blood plus homologous organisms (0.1 cc.)	+	+	0	0	0	0	0
0.5 cc. blood plus sulfanilamide plus organisms	+	+	0	0	0	0	0
0.5 cc. normal blood plus organisms	+	+	+	+	+	+	0
0.5 cc. normal blood plus sulfanilamide plus organisms	+	+	+	+	+	+	0
Patient 2							
0.5 cc. blood plus homologous organisms (0.1 cc.)	+	0	0	0	0	0	0
0.5 cc. blood plus sulfanilamide plus organisms	+	0	0	0	0	0	0
0.5 cc. normal blood plus organisms	+	+	+	+	+	0	0
0.5 cc. normal blood plus sulfanilamide plus organisms	+	+	+	+	0	0	0

+ = growth at 24 hours; 0 = no growth at 24 hours.

*The 10^{-7} dilution contained 6 organisms in 0.1 cc.

amide, were highly bactericidal for the homologous organisms. This indicates that recovery was accompanied by the development of specific antibody in high concentration.

In patients with hemolytic streptococcal bacteremia there is usually a clearing of the blood, with or without the localization of abscesses; the leukocyte count increases, the temperature declines, and the local lesion shows signs of regressing.

When meningitis is present, it is usually necessary to drain the primary focus of infection, to use blood transfusions and to keep the concentration of sulfanilamide in the cerebrospinal fluid high — at least 10 mg. per cent. When these procedures are carried out the results are often nothing short of remarkable. Other hemolytic streptococcal infections respond favorably to chemotherapy, and this should be employed without hesitation.

In gonococcal infections, the drug has a profound effect in that it creates an environment in which gonococci have difficulty in surviving. The synovial fluid is sterilized, and in many cases the local focus in the genitourinary tract is likewise sterilized. Here again the question of dosage is important, since an optimum concentration of at least 5 mg. per cent must be reached in the blood and synovial fluid.

Meningococcal meningitis can be strikingly influenced by sulfanilamide, and in some cases complete cures are accomplished within a few days. It has not been necessary to use antimeningococcal serum in the cases we have studied, nor have we injected the drug into the spinal canal. It is essential, however, that the drug be given in large amounts so that optimum concentrations in the blood and cerebrospinal fluid can be obtained.

The course of infections of the urinary tract due to *B. coli, B. influenzae, B. proteus* and *Staphylococcus aureus* can be changed with the use of this drug. It is definitely bacteriostatic, and in some cases the urine fails to support the growth of these organisms as long as the drug is given. When it is withdrawn, there may be an exacerbation of the infection with a reappearance of organisms in the urine. Such observations tend to show that the normal body-defense mechanism for destroying organisms must be operative in the final destruction of organisms in the urinary tract.

CONCLUSIONS

There is evidence that sulfanilamide exerts a profound effect in vitro and in vivo on the rate of growth and multiplication of various microorganisms, such as hemolytic streptococci, pneumococci, meningococci, gonococci and the organisms commonly found in infections of the urinary tract.

There seem to be two features essential for optimum results: the organisms must be brought in contact with a sufficient concentration of the drug to produce optimum bacteriostasis; the normal defense mechanism of the body must be operative in order to rid the body completely of the infective agent.

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DISCUSSION

DR. EDWIN H. PLACE, Boston: The results from sulfanilamide that have been reported are of extraordinary interest to us all. They open up a field of therapeutic endeavor which we have very much needed. At the South Department of the Boston City Hospital the results we have obtained with sulfanilamide seem to support those recorded here.

In scarlet fever the benefits of therapy are not easily demonstrated. Perhaps the most illuminating evidence

that we have had developed in our scarlet-fever ward, where during 1937 the death rate dropped to a level that had never before been reached. It was 0.14 per cent, as I remember it, or 1 death in 760 cases. In that period no patient died with septicemia, an event which is, of course, unique. Last year the Boston death rate for scarlet fever dropped to the lowest point ever reached, but as regards the use of sulfanilamide, it seems somewhat significant that our death rate dropped to an even greater degree; although we had about 30 per cent of the patients reported in Boston, we furnished only 11 per cent of the deaths. In the past the hospital has had about 30 per cent of the patients and 50 per cent of the deaths, the more severe cases probably going to the hospital, but with this form of chemotherapy ostensibly applied more in the hospital than in private practice, the results have been reversed.

Early in the spring of 1937, during the epidemic of meningococcal meningitis, we began to treat our cases with sulfanilamide by mouth. Previously the mortality rate with serum therapy had been about as usual, that is, a little less than 50 per cent. The year before, the mortality was 47.7 per cent in our wards, and 48 per cent in Massachusetts. In 1937, after a few preliminary cases in which serum was also given, we began sulfanilamide treatment, and have used no serum in the cases admitted since that time — a total of 26 cases, with only 3 deaths. The epidemic has been stopped.

The effects of sulfanilamide are strikingly shown in the rapid improvement — much more rapid than we ordinarily see with serum. In more than half our cases the cultures from the spinal fluid taken within the first twenty-four hours were negative. In all the cases cultures were sterile by the end of the fifth day and remained so, and all but one or two were sterile by the end of the third day. These findings are in striking contrast to what we find following the use of specific serum, when cultures are frequently positive for five, ten, fifteen or even twenty-five days, and relapses are not particularly rare.

We use sulfanilamide in large doses, — the average is 100 gr. every twenty-four hours, — and continue it for two weeks. We do not dare to use smaller doses or to stop them earlier. I am strongly inclined to believe that we use more than we need to, and that in view of the rapid improvement that occurs we do not need to continue it so long. We have had no relapses. I presume that in the future we can cut down both the duration of dosage and the amount given.

The ill effects were not striking. We had no leukopenia, and only 1 case of severe anemia. On the whole, I believe that we can look forward with great hope to the use of sulfanilamide in the treatment of these serious infections.

Dr. Champ Lyons, Boston: I have just concluded a study of sulfanilamide from the surgical standpoint. For that reason I shall speak chiefly of its use in hemolytic streptococcal infections.

In the laboratory we have confirmed the bacteriostatic effect of the drug. In addition to this action, streptococci which have been grown in mediums containing sulfanilamide can be shown to have suffered an attenuation of their virulence that is often sufficient to permit the streptococci to be killed by the body even in the absence of specific antibody. On the other hand, the presence of antibody always enhances the bactericidal effect observed with sulfanilamide, so that the combination of sulfanilamide and specific antibacterial serum is more effective than is either one alone.

I have come to realize that the blood-sulfanilamide level of 5 to 10 mg. per cent is adequate only for those cases which have already developed antibacterial antibody prior to treatment. A 10-mg. level has been maintained for three days and longer in patients with bacteremia and no antibody, without any clear effect on the persistently positive blood cultures. We have had patients die with hemolytic streptococcal bacteremia in spite of receiving what we have been told constitutes adequate sulfanilamide therapy. Patients with hemolytic streptococcal bacteremia and no antibacterial antibody have been effectively treated by combining sulfanilamide and immunotransfusion from selected donors.

It may be impossible to secure an immune donor for certain strains of streptococci. We are getting better results in the treatment of patients with no antibody by using larger doses of sulfanilamide, and I believe that a blood level of 25 mg. per cent should be used when no immune serum is available. There have not been enough of these cases for us to evaluate the efficiency of the greater dosage, but it would seem that the bacteremic patient with no antibody has a better change of recovery with the higher blood level of sulfanilamide. However, the toxic manifestations of the drug when used in this dosage make me prefer to use antibody if it is available.

A point to emphasize is the fact that patients treated with sulfanilamide early in the course of their infection frequently fail to develop antibacterial antibody as a result of the infection. If they are to be effectively treated they must be kept under observation until the broth cultures of swabs from their lesions are consistently sterile. Patients who have received inadequate treatment may develop a persistent nonsuppurative or suppurative inflammation of the lymph nodes that prolongs their convalescence for weeks or months.

In conclusion, I think it is important to regulate the dosage of sulfanilamide in relation to the presence or absence of antibody, wherever possible.

THE SIGNIFICANCE OF LATENT FORMS OF TUBERCULOSIS

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ONE of the most important recent advancements in the field of tuberculosis consists in the development of our knowledge of its pathogenesis. The processes are now so well understood in their relation one to another that it is possible, after infection has occurred, to anticipate the paths along which succeeding lesions may establish themselves. Whether the inception of clinical disease is related mostly to infection from without or to a spread of infection from foci previously established in the body is still being debated, but the endogenous route of reinfection is the vital one in many cases, and it is clear that progressive and fatal tuberculosis practically always involves a succession of new lesions related to the dissemination of infection from pre-existing ones. It is also clear that in almost all serious cases the lesions at some recent or remote time passed through a period or periods of latency, varying from a few weeks to many years. The revelation of these latent phases is due largely to the widespread practice of periodic health examinations and surveys of large groups of people with routine roentgenograms of the chest. These methods have proved their unique value in discovering the presence of tuberculous lesions before they have passed into the symptomatic stage. At the same time many new problems have been raised, particularly with regard to the significance of the lesions in the lives of those who harbor them. Experience shows that some of the findings are to be disregarded while others are of potentially great danger, and that proper identification and treatment of the latter group is the most effective way of preventing advanced and fatal tuberculosis. Judging the significance of latent lesions is difficult, and tragic mistakes are numerous.

Conceptions of what constitutes latent tuberculosis differ. The simplest clinical definition, which to my mind is the only legitimate one, is: the presence of any tuberculous lesion which fails to produce symptoms of its presence. By this I mean both subjective and objective symptoms. A lesion is no longer latent when it causes a patient to suffer from undue fatigue. Likewise, the gradual loss of weight from this cause, even though the patient is not aware of his failing, is an indication that the latent stage has been left behind. The definition is somewhat arbitrary; nevertheless, it furnishes an important clinical distinction because it comprises in one group for careful consideration a large number of lesions which may or may not require treatment, leaving in another extensive group those cases of obviously active and clinically important disease in which treatment is always indicated.

A latent tuberculous lesion may or may not be demonstrable. In case it cannot be discovered by our various methods of examination, it is regarded as concealed or occult. It is equally true that an occult lesion may or may not be latent. For example, a sore lump in the neck which is red and palpable and represents a tuberculous node is a clinically active lesion, but a tuberculous node found by palpation in a patient without symptoms is a latent lesion. A tuberculous node buried in the mediastinum of a patient without symptoms is both latent and occult. An infiltration in the lung producing no symptom is, by this definition, latent even though rales may be heard over it and the roentgenogram may clearly demonstrate its presence. The finding of crepitant rales has no direct relation to the clinical activity or latency of the pulmonary lesion. Many fibrotic and thoroughly stabilized lesions, which represent no significant hazard for the patient, give rise to rales. On the other hand, many very dangerous latent lesions produce no audible rales even though the roentgenographical indication is clear.

As implied above, latent lesions may be early or of long standing, inflammatory or caseous, fibrotic or calcified. While still latent they may during a period of time prove to be stationary, retrogressive or progressive. If the lesion is continuously progressive, the phase of latency is eventually passed and the patient develops symptoms. It should be repeated that some of these lesions are obsolete and innocuous, while at the other extreme some constitute a grave threat to health and life, a threat which may be either immediate or remote.

While considering terminology, we may digress to mention the generally employed distinction of tuberculous infection and tuberculous disease. The former is usually understood to include the cases in which the only evidence is a tuberculin reaction with or without demonstrable small lesions which do not necessitate treatment, while tuberculous disease is meant to include all that is clinically significant. This distinction has its usefulness for practical purposes. Nevertheless, from the scientific viewpoint it is a confused conception without a

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rational basis. Infection, strictly speaking, is the process of implantation and dissemination of bacilli in the tissues of the body. If by chance the implanted bacilli are destroyed in situ or removed without causing a change in tissue, the process begins and ends with infection. The result of infection, if the implanted bacilli remain viable, is a lesion. It is fundamental, therefore, that the process of infection and its effects are different things. In most cases the effect is a small lesion or chain of lesions which remains localized and becomes permanently encapsulated without harm to the bearer's health. In some there is a slight and temporary impairment of health before the lesions are arrested, while in a few the infection is progressive and the resulting lesions produce the harmful and deadly effects with which all are familiar. It should be clear, therefore, that after the fact of infection has been established in any patient, the physician should immediately think in terms of lesions and their actual and probable effects. This will lead him to a careful consideration of the many latent phases of the disease and divert him from the fallacy that all tuberculosis is divided into two parts, that which is making the patient sick and therefore needs treatment, and that which is not making the patient sick and therefore needs no treatment.

When confronted with a patient who harbors a latent tuberculous lesion, the practical problem is to judge the potentialities of the lesion and to make fine discriminations as to the probable outcome under varying conditions. It is unjust to penalize the patient with an innocuous lesion by advising a period of treatment; on the other hand, it is equally essential not to mislead the patient with a threatening lesion by diverting him from the treatment which will save his health and life. In the latter case the obligation is in reality twofold, since early and proper treatment also prevents the transmission of the infection to contacts. This is indeed a medical problem of the greatest urgency. The necessity of treatment for the symptomatic case with pulmonary cavitation is self-evident, but the judgment of these finer problems requires wisdom of a superior order. The criteria of judgment are of varying reliability. In some situations they are purely empirical, while in others they are quite objective and fairly exact. The future will see much refinement along this line, but even now the proper use of existing criteria can accomplish much good. The only fixed rule is that the study of each case shall be careful and thorough.

Guiding Factors

Age. The age of the patient harboring a latent tuberculous lesion has a bearing on the outcome which is at times paramount. Several contrasts may be mentioned. Considering groups of people who have been infected with the tubercle bacillus, Drolet[1] showed that during the period 1930-1932 the death rate among infants in New York City was 1297 per 100,000 per year. This devastating rate, which is five to thirty times as great as that of other ages, is usually lost to view because mortality rates are reported, not on the basis of infected groups, but for the whole community. The general experience is verified by the eight-year study of Brailey,[2] who observed in Baltimore a mortality of 34 per cent and 10 per cent, respectively, among colored and white children found to be tuberculin-positive before two years of age. Fatalities in infants are due chiefly to generalized lymphogenous and hematogenous lesions, usually acute. Throughout later childhood, for some unknown reason, tuberculosis takes a relatively low toll, but during adolescence and early adult life serious and fatal disease again asserts itself, this time in the form of pulmonary tuberculosis and its sequences, including tuberculosis of the larynx and of the intestines. The early pulmonary lesion in young people is often latent for a time but tends strongly to progress into a more or less acute caseating and excavating form of tuberculous pneumonia, while in the later decades of life we see more of the slowly progressive chronic fibroid forms.

Sex. It is during adolescence that the influence of sex asserts itself most strikingly. Tuberculosis in young girls, more than in boys, is notoriously liable to be of the acute exudative type — unstable, progressive and highly fatal. In women past thirty, on the other hand, latent lesions do not seem to progress so often as they do in men of similar age. Living conditions at this point probably have a stronger influence than has age.

Race. In most communities Negroes during adolescence and early adult life show an intensification of the general tendency to the acute exudative forms of pulmonary tuberculosis. This appears two or three years earlier in the adolescence of Negroes than it does in Whites. In our experience, also, the Negro shows a greater predisposition to the lymphogenous and hematogenous dissemination of the infection.

Environment and Occupation. Epidemiological studies show clearly that low social economic status and exhausting occupations favor the development of progressive and fatal tuberculosis. A striking contrast is noticed between the mortality among professional men and that among unskilled male workers, the rate being ten times as high in the latter group.

Recency of Contact. An infant in intimate con-

tact with a positive sputum case in the home is in great danger of developing tuberculosis. Close contact during or shortly before adolescence appears to be a factor in the development of progressive pulmonary lesions. In later life, however, contact seems to have a decreasing influence on the chance of a latent lesion's becoming progressive.

Allergy. Much study has been given to the question whether pre-existing allergy and therefore a pre-existing tubercle is a favorable or unfavorable influence on the fate of newly appearing lesions. Careful studies seem to indicate that among large groups of healthy adults more lesions develop in the lungs, after exposure to the infection, among those who previously failed to react to tuberculin. The inference is that long-standing allergy is associated with an increasing relative immunity against the tubercle bacillus. My own experience does not contradict this. It seems to me, however, that the influence of allergy is often overemphasized and that more decisive factors include the general health of the patient, his race, sex and age, and the time at which he acquires his primary infection. The intensity of the tuberculin reaction is no indicator of the probable behavior of latent lesions.

Time of Primary Infection. As stated, infection in infancy is followed by a high mortality, but this does not seem to be true at later age periods, if our own observation of nurses in the Bellevue Hospital Training School has any meaning. During eight years' study, some 300 have developed skin hypersensitiveness after entering the school. This allergic change must indicate a primary infection or the intensification of a very low allergic state. If the former, had these nurses reacted like infants we should have expected 20 to 30 deaths from generalized tuberculosis during the period of study. The fact is there has not been a single death, suggesting that increasing age means increasing natural resistance, or at least that some factor associated with increasing age operates favorably for the infected person.

TYPES OF LATENT LESIONS

Size. Sanatorium experience indicates a relation between the extent of lesions and the prognosis. In small, latent lesions this is somewhat less evident but is still of importance. Extensive tuberculosis of the mediastinal lymph nodes in a young child or an adolescent Negro is much more likely to portend later dissemination through the lymph and blood streams than is the involvement of a single node. Likewise, the extent of involvement in the lung parenchyma has a definite bearing on the outcome.

Distribution. Generally speaking, a single lesion confined to one organ is potentially less dangerous than multiple lesions in various organs. The necessity, therefore, of recognizing the pathways of spread in the body and of searching carefully for other lesions set up through these pathways is self-evident. It must always be remembered that while one lesion may be demonstrable, a number of others may be concealed.

Location. The site of a latent lesion may have a good deal to do with its ultimate fate. I again emphasize the tendency to hematogenous disseminations in cases with extensive lymph-node involvement as contrasted with those cases where only the parenchyma of the lung is affected. In my experience, the site of a lesion in the lung has little to do with its ultimate fate. Small basal infiltrations with little or no excavation have healed just as well as have those near the apex.

Primary Infection or Reinfection. It is sometimes said that the lesions resulting from primary infection with the tubercle bacillus run a uniformly benign course. Neither Lincoln,[8] in her experience in the Children's Medical Service at Bellevue Hospital, nor I have been able to find any evidence to bear this out. A primary focus in the lung, of course, is seldom a direct cause of death, but in infants, at least, the immediate consequences of dissemination from the primary focus may be serious and fatal. In brief, our experience leads us to the conclusion that tuberculosis should be treated in the same manner whether it follows primary infection or reinfection, judgment being based on the extent and character of the lesion and on the other factors described.

Tissue Reactions. It is clear to everyone that an old, latent, fibrous tuberculous lesion has a meaning very different from a latent bronchopneumonic lesion of similar size but recent origin. In general, it may be said that recent inflammatory lesions are very unstable, particularly in young people, and more particularly in young women. Necrosis with caseation and liquefaction make the potentialities more serious, because of the greater likelihood of dissemination through the blood stream if such lesions are in the lymph nodes, or through the bronchial pathways if they are in the pulmonary parenchyma. The fate of a fibrous lesion depends partly on the amount of enclosed caseous matter. A clean tuberculous scar seldom breaks down. Calcification is usually looked upon as a measure of healing of tuberculous lesions. It should be remembered, however, that only the caseous part becomes infiltrated with calcium salts; in other words, this is a reaction in necrotic tissue which harbors or has harbored numerous tubercle

bacilli. Rather than as an indication primarily of healing capacity, therefore, I look on the extent of calcification as an index of the extent of pre-existing caseation, realizing that such foci, although appearing hard on the x-ray film, may still be rather cheesy or chalky and capable of liberating tubercle bacilli. This, no doubt, is one explanation of the more frequent development of pulmonary tuberculosis in adolescent children who show such extensive calcified deposits.

Studies of the blood leukocytes and of the sedimentation rate of the erythrocytes have a limited usefulness as criteria of the meaning of latent tuberculosis. A deviation from normal, especially if the observations are taken at frequent intervals, may be significant, but normal findings do not exclude the possibility that a latent lesion is dangerous or even actively progressive.

An ulcerating latent lesion always constitutes a threat of progressive disease. Minimal ulcerating lesions of the lung produce little discharge into the bronchi, and this may unconsciously be raised and swallowed. The patient naturally reports that he has no sputum. Careful instructions may lead him to produce small particles in the morning which contain tubercle bacilli, or they may be found in the gastric washings.

CORRELATION OF FINDINGS

The significance of a latent tuberculous lesion is judged by a consideration of the factors enumerated and verified by a period of observation under suitable conditions. Thus, the discovery by the routine roentgenogram of a small, soft patch of tuberculous infiltration in the lung of a high-school girl should be considered of serious significance. Blood studies and gastric washings may be negative; nevertheless, the tendency of such a lesion in such a subject to spread rapidly is an indication for confinement to bed, where observation and treatment may be carried out as I have described elsewhere.[4] The lability of these lesions in young people is too often unappreciated. The most valuable means of observation is the roentgenogram. This examination is repeated weekly for three or four weeks, and then at lengthening intervals until stability of the lesion seems established; during the first year a month between roentgenograms is not too brief a period. At the opposite extreme, a hard, fibrous-looking lesion in a man of forty does not usually portend great danger, and a routine examination every two to six months may be the only requirement. Individual variations are unlimited. Experience is necessary for proper judgment, since the task is to assess each case according to the lesion and its biological setting. It is to be remembered that there is scanty evidence for natural variations in the virulence of the tubercle bacillus, but that there is ample indication of wide differences in the fertility of human tissues for the germ. If the tissues are judged to be fertile and the lesion to be budding, prompt and energetic action must be taken to arrest its growth. To wait to be convinced by its clinical efflorescence is to court disaster.

SUMMARY

Many latent tuberculous lesions are discovered by routine roentgenographic examination of the chests of apparently healthy people.

The significance of these lesions is judged individually by a number of factors including the age, sex and race of the patient, his environment and occupation and the recency of contact.

The existing or previous state of allergy has less bearing on the probable fate of the lesions than other factors.

Advancing age seems to be associated with increased resistance against infection.

The character, size and distribution of the lesions are of greater importance than their relation to primary infection or reinfection.

Sound judgment depends on a careful correlation of all factors which can be identified and estimated in the individual case.

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Discussion

Dr. Henry D. Chadwick, Boston: It has been a pleasure to have Dr. Amberson with us today and to hear him discuss this very important phase of tuberculosis, which he can do so well as a result of his great experience in the treatment of this disease.

I am entirely in accord with his conclusions, and can only give some evidence in support of them as a result of the analysis of the large number of cases of tuberculosis in childhood that were discovered during the period in which we carried on an extensive program in the schools. Beginning in 1924 and continuing for ten years, we had groups of investigators examine school children by performing a tuberculin test and taking an x-ray picture of the chests of those that reacted. The figures which I am about to give you have been abstracted from a paper recently written, but not yet published, by Dr. David Zacks, who has had charge of this clinic program for several years.

During the ten-year examination period 400,000 children were given the tuberculin test and 100,000 of them were x-rayed because they reacted to the test. The x-rayed

cases were divided into three groups: those that showed definite evidences of tuberculosis; those in which the evidence was not conclusive which were therefore called suspicious; and those that were negative on x-ray. The patients found to have tuberculosis and those classified as suspicious have been followed for periods varying from one to twelve years, or an average of four years. Of the entire number of children, approximately 500, who were found to have pulmonary tuberculosis in some form, 72 per cent had no symptoms at the time of discovery. The diagnosis was made entirely from the roentgenogram. Twenty-three per cent had some symptoms, and of that portion 6 per cent had tubercle bacilli in the sputum. In other words, about 75 per cent of the group had no symptoms on which to make a diagnosis. They presented the so-called latent or symptomless type of tuberculosis. Following through these cases, we find that 63 per cent were progressive during the period of observation, and that 22 per cent of these patients are dead.

This shows that latent tuberculosis is a very serious condition, and the difficulty is to know what to do about it. You see a well-developed girl or boy, — there were twice as many girls as boys in this series, — who appears to be perfectly well, with good flesh and color, without symptoms on which to make a diagnosis. They prebe by x-ray that there is a small bronchopneumonic patch in the lung — usually in the upper half, although it may occur anywhere. You wonder whether it is significant. Only by observation over a long period can we get the evidence from which to conclude that the apparently innocuous lesions are serious when found and should be under constant observation and treatment from that time on. The patients should be excluded from school immediately and given plenty of bed rest. We have usually found it necessary to give some form of collapse therapy. We tried bed treatment consistently in the sanatoriums, keeping children in bed for a year and sometimes two years, but with little or no change in the lesion. It is only during the last few years, when we have supplemented bed rest with a pneumothorax, that we have begun to get better results.

There is one important thing I should like to emphasize: When we find by x-ray a soft bronchopneumonic lesion we cannot at once say that it is tuberculous, even if a tuberculin test is positive, because bronchopneumonia resulting from so-called grippe infection oftens occurs in school children. We learned by experience in the early years of our work that it was necessary to follow our examination with further x-rays in two or three weeks in order to distinguish the nontuberculous lesion of bronchopneumonia from the tuberculous lesion. Nonspecific lesions resulting from colds — and in most of these cases we find a history of a cold — disappear within two or three weeks, while tuberculous lesions remain unchanged over a long period. So that this is something one must keep in mind when seeing in any film a small bronchopneumonic lesion.

Dr. Amberson has rightfully emphasized the seriousness of a tuberculous infection, even in infancy. After infancy and up to the tenth year these lesions of tuberculous origin are much less serious, and are very apt to retrogress, leaving a lesion which may or may not become calcified, depending on whether or not caseation takes place. In the second decade, lesions of similar appearance are much more likely to progress unfavorably, as shown by the cases studied, two thirds of which have developed advanced disease, and a considerable percentage of which have had a fatal termination. Therefore, in considering prognosis and treatment, we must take into account both the age and the sex of the patient.

I do not believe that the site of the lesion makes any difference as to whether it is likely to progress or to retrogress. Calcification, as has been said, is evidence only of the deposit of calcium in a necrotic area and gives no indication as to how many other foci of tuberculosis are associated with the lesion. Infection follows the lymph nodes; we may find one lymph node near the root of the lung to be well calcified, but we must remember that it is only one of many which are intimately connected, and that the infection is easily conveyed by the lymph from one diseased node to others in the chain. We may have a group of caseous lymph nodes in the mediastinum that cannot be seen on the roentgenogram.

As to the effect of infection on resistance, I agree entirely with what Dr. Amberson has said. Whether or not progressive disease develops depends very largely on the amount of infection. The more lesions the more bacilli, and the more opportunity for a transfer of the infection to other sites in the lung, either by the blood stream or by the bronchial pathways.

A few years ago Dr. Pope studied a group of 800 children that had calcifications in their lungs after five years had elapsed, and found that 3.7 per cent of them had developed the adult type of tuberculosis, while of a group of 400 children in whom the only evidence of tuberculosis was a positive tuberculin test, only 0.7 per cent developed the adult type. In other words, five times as many of those with calcified lesions in the lungs developed the adult type of tuberculosis in the same period of time. To continue further, he analyzed a control group of 900 children who were negative to the tuberculin test and had had no x-ray, and found that only 0.22 per cent had developed pulmonary tuberculosis in the same length of time. So it comes down very largely to the number of tubercle bacilli that the individual is carrying around in his tissues. Sex is an important factor since we find that girls are more prone than are boys to develop tuberculosis during the second decade.

Death rates, while they are significant, do not tell the whole story. They are high during the period of adolescence, but we find in our series that an average period of three years elapsed between the x-ray diagnosis and the appearance of symptoms. Three years of latency, in other words, was the average period before tuberculosis became manifest. So that a boy or girl in the teens may receive the infection and develop a focus of disease that remains latent until the third decade, and the death must be listed as occurring in that period.

We have been trying for many years to get tuberculosis under treatment in its minimal stage, but we have not progressed very far. We find that from 80 to 90 per cent of admissions to sanatoriums today, as in the past, are moderate or advanced cases. We get very few minimal cases by ordinary methods of examination; that is, if we wait for the patient to develop symptoms sufficiently noticeable to send him to a physician. It is only when we examine the contacts of cases of tuberculosis, before any symptoms develop, or when we make routine x-ray examinations, that we find truly minimal cases.

I am very glad that this subject was selected by Dr. Amberson for discussion before this society, because it is one of the most important in the field of tuberculosis.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 24411

PRESENTATION OF CASE

A forty-nine-year-old Swedish machinist entered the hospital with the complaint of swelling and pain of the face and neck of five weeks' duration.

Five weeks before entry he had a sudden, sharp pain in the left flank which lasted for only a few moments but persisted as a dull pain for a period of two days. It was aggravated by coughing or straining, and after the two-day period spread up into the left chest and centered in the region of the left shoulder blade. After two more days it spread to the head, face and neck, and the right side of the face and neck became swollen and tender. He also had a sore throat at that time. The pain was aggravated by stooping or lying down, and he noticed that one of the neck veins over the swollen area was engorged. The swelling was more pronounced in the morning and gradually decreased somewhat during the day; it gradually spread to the left side of the neck and to the right shoulder and arm. He continued working, however, although his physician could give him no relief. Three days before entry he began to have a persistent cough productive of small amounts of white phlegm without blood. The following morning he awoke with much more swelling than before and noticed that he was somewhat dyspneic. The swelling was so marked that he could not open his eyes, but as usual it subsided somewhat after he got up. He had no orthopnea or other cardiorespiratory symptoms, and no chills, fever, dysphagia or hemoptysis.

For a period of fifteen years, ending two and a half years before entry, he had had symptoms of stomach ulcer; and finally, following two large hematemeses, a subtotal gastrectomy was performed at an outside hospital. The pathological report on the specimen stated that the lesion was a penetrating peptic ulcer, measuring 2 cm. in diameter, located on the lesser curvature. Following the operation the patient was completely relieved of his symptoms, although he remained on a bland diet. During the few months before entry he had noticed some weakness and loss of appetite but had not lost weight. Up until seven years before entry he had regularly consumed a pint of "spirits" daily, but since then he had not drunk at all. His family history was negative.

Physical examination revealed a fairly well-developed but rather thin man in mild discomfort. The face, neck, arms and upper chest were darkly flushed and appeared very full in comparison to the rest of the body. The veins of the neck were engorged. Soft, tender movable masses could be felt on both sides of the neck, more marked on the left. The fullness of the neck extended down to the clavicles with obliteration of the suprasternal and supraclavicular fossae. The veins of the upper anterior part of the chest, both arms and both shoulders were distended. The trachea was displaced somewhat to the right. There was a soft, movable node in the left axilla, measuring about 2 cm. in diameter. No other superficial lymph nodes could be palpated. The heart and lungs were negative except for a few questionable rales in the right lower lung field posteriorly and laterally. The blood pressure was 125 systolic, 75 diastolic in both arms. The right pupil was slightly larger than the left. The abdomen was negative.

The temperature was 98.6°F., the pulse 90. The respirations were 20.

The urine examination was negative. The blood showed a red-cell count of 5,160,000 with 80 per cent hemoglobin and a white-cell count of 10,000 with 72 per cent polymorphonuclears, 17 per cent lymphocytes, 9 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The stool was guaiac negative, and the blood Hinton test was negative.

An x-ray of the chest showed a lobulated soft-tissue mass in the right upper mediastinum, probably placed anteriorly. The trachea was slightly displaced to the right, indicating that a mass was probably present on the left. Both costophrenic angles were obliterated. A gastrointestinal x-ray series showed about three-fourths of the stomach to have been resected. There was marked thickening of the gastric rugae and slight pouching of the anastomosed jejunum. The anastomosis functioned freely, and there was no evidence of cancer.

A cervical lymph node was removed for biopsy on the third day.

DIFFERENTIAL DIAGNOSIS

DR. DONALD S. KING: I am sure that you have made up your minds as to the diagnosis in this case. At first it seems simple, but I have learned not to trust these pathologists, and we must study the facts as carefully as we can. The picture is primarily that of upper mediastinal obstruction. There were at first a few symptoms referable to the left flank and left shoulder, but

these disappeared quickly. There was a past history of overindulgence in alcohol but since no alcohol had been taken for seven years, I am willing to forget that part of the story. There were also symptoms of a possible peptic ulcer, which I shall consider later. The weakness and anorexia can be ascribed to any condition causing the mediastinal obstruction. The pressure in the upper mediastinum was principally on the superior vena cava. We have no evidence of pressure on the esophagus or involvement of the phrenic, recurrent laryngeal or vagus nerve. The right pupil was slightly smaller than the left, but this is not sufficient evidence for involvement of the sympathetic nerve. A few days before admission there was cough and dyspnea, probably due to pressure on the trachea or bronchi.

We are looking then for something which is pressing principally on the superior vena cava. We are helped because we know that this something also involved the cervical lymph nodes, either primarily or by metastasis, and we assume that the answer to the problem is given by biopsy of one of these cervical nodes. This rules out mediastinitis, mediastinal abscess or thrombosis and brings us to the question of tumor, primary in the lymph nodes or metastasizing to them. We can throw out such benign tumors as aneurysm, substernal thyroid, dermoid cyst, and so forth. The nodes in the neck were bilateral, soft, freely movable, and so far as we know, non-tender. This description is not characteristic of carcinomatous lesions. The chest x-ray shows a bilateral process which is lobular and in the anterior portion of the upper mediastinum. The description as given sounds as if the shadows were those of glandular masses.

What are the possible relations between these masses in the chest and the nodes in the neck? I can think of three possibilities. First, the mediastinal mass may be the primary source of the metastases in the neck. If this is so with what kind of mediastinal tumor may we be dealing? The x-ray is consistent with bronchiogenic carcinoma which frequently metastasizes to the cervical nodes, but the symptoms are not those which we would expect to find with such a growth. It is interesting that out of more than 150 proved cases of carcinoma of the lung we have had only 1 case of upper mediastinal obstruction with pressure on the superior cava and edema of the face. The shadow could be that of carcinoma of the esophagus with metastases, but carcinoma of this size involving the esophagus would almost certainly give dysphagia and is in my opinion ruled out. The upper mediastinal tumor could be of a sarcomatous nature with metastases.

The second possibility is that the mass in the mediastinum and the nodes in the neck are both metastatic from some other source, possibly the nasopharynx, esophagus or prostate. Because of the gastric resection we must also think of cancer of the stomach as the possible source of metastases to the mediastinum and neck, but the story as given seems to rule out this possibility.

The third possibility is a primary disease of the lymph nodes involving these structures in both the neck and the mediastinum. The blood studies rule out leukemia. I do not believe that it is tuberculosis of the nodes. The Hinton test was negative so that syphilis is unlikely.

This seems to me to leave as the most logical diagnosis the involvement of the lymph nodes by one of the types of disease classified under the name lymphoma. I should like to know how Dr. Hampton feels about the mediastinal shadows from the x-ray standpoint, whether he agrees that the lesions are consistent with lymphoma. I was not supposed to see all the x-ray films in this case, but by mistake I did see the film which was taken after the x-ray treatment; the fact that the masses had disappeared after comparatively small doses of x-ray also suggests the diagnosis of lymphoma.

DR. AUBREY O. HAMPTON: The lesions are perfectly consistent with lymphoma.

DR. KING: And not quite typical of primary pulmonary carcinoma.

DR. HAMPTON: No.

DR. KING: Could they be metastatic?

DR. HAMPTON: Yes.

DR. KING: But perfectly consistent with lymphoma, or lymph-node lesions of some kind.

DR. HAMPTON: He has large nodes and what appears to be a small amount of fluid in the costophrenic angle.

DR. KING: That would not help you either way.

DR. HAMPTON: No; but you can be sure that the tumor is malignant.

DR. KING: I assume there has been x-ray treatment. I am sorry I saw this film. The patient had had x-ray treatment in the meantime.

DR. HAMPTON: Your diagnosis up to the present time is what?

DR. KING: It is lymphoma, but I have not convinced myself as to the type.

DR. HAMPTON: I know the answer from hearsay. He did have radiation, 1200 r front and back over the chest, more than the lymphoma dose, but not so much as we should ordinarily

give if we were treating carcinoma. Furthermore, he showed more improvement than one would expect if it were carcinoma. So you still think it is consistent with lymphoma? Do you want to make other suggestions? I shall leave it up to you.

DR. KING: I am interested in the stomach.

DR. HAMPTON: I cannot say this lesion of the stomach is cancer, although such a diagnosis is suggested by its location. It is in the prepyloric area.

DR. KING: You cannot find cancer now, two and a half years later?

DR. HAMPTON: Not in his stomach. I think there is malignant tumor in the chest, however.

DR. KING: The pathological examination at the time of operation did not show cancer, although I realize that you would like to prove it.

DR. HAMPTON: In this particular area of the stomach, the prepyloric region, there have been several cases where the lesion has been reported as benign and the patient died of cancer several years later. So if you want my diagnosis I should say cancer of the stomach.

DR. KING: And you would explain the mediastinal shadows by metastases from the stomach which cleared by x-ray treatment?

DR. HAMPTON: Yes. We have seen enough cancers that have cleared up after that dose of radiation to make it possible to say that some cancers do respond to the lymphoma dose.

DR. KING: You are going on the law of chances then that the lesion in the stomach is cancer and not ulcer.

DR. HAMPTON: Yes.

DR. KING: I have a pathological report that says it is not cancer and the pathologist actually had the specimen in his hands.

My diagnosis is lymphoma, — probably not lymphosarcoma, — of the Hodgkin's type.

PREOPERATIVE DIAGNOSIS

Lymphoblastoma.

DR. KING'S DIAGNOSIS

Lymphoma, Hodgkin's type.

ANATOMICAL DIAGNOSES

Colloid carcinoma of the stomach with metastases to mesenteric, bronchial and cervical lymph nodes and bone marrow.
Operative wound: subtotal gastrectomy.
Bronchopneumonia.
Myelophthisic anemia.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. King's skepticism in regard to pathologists is well borne out in this case. Resection was done at another hospital, and the specimen examined there and reported as benign ulcer. When the patient came in here one of the cervical lymph nodes was biopsied; it showed a type of adenocarcinoma which suggested very strongly that the primary origin was somewhere in the gastrointestinal tract, perfectly consistent with cancer of the stomach. We then went searching for the original specimen and finally had a chance to look at it. It showed what to my eye was unquestionably a cancerous process. There was a diffuse infiltration of the wall of the stomach with small signet-ring cells which could be very easily mistaken for mononuclear phagocytes, but this is a very common type of growth in cancer of the stomach and one we constantly must be on guard against so as not to miss. At the time of autopsy we could not definitely make up our minds whether there was still cancer in the stomach, although one area was so indurated that we thought so. Sections from that area showed small undifferentiated cells with occasional signet-ring appearance. It is rather characteristic of some of the stomach tumors that the primary tumor is totally undifferentiated. You will hunt through a great many sections and not see a sign of gland, whereas in metastases you find well-defined gland formation. That was the case here in the majority of the metastases that we found.

As for the mediastinal tumor, I cannot be sure. The autopsy gave not the slightest help. There was none!

DR. KING: Was there anything in the mediastinal lymph nodes?

DR. MALLORY: They were all small and of normal size and consistence except for two small bronchial nodes which contained tumor. There were metastatic nodules in the neck, so small that they were not grossly palpable.

DR. KING: Why did he die?

DR. MALLORY: His terminal course was progressive anemia, cachexia and death. He had a terminal bronchopneumonia. At the time of death the red-cell count was below 1,000,000.

A PHYSICIAN: Were his bones examined?

DR. MALLORY: Yes. They contained metastases everywhere.

DR. HAMPTON: I should have mentioned that the pelvis showed metastases; this is still consistent with lymphoma so far as the x-ray picture goes.

CASE 24412

PRESENTATION OF CASE

A thirty-nine-year-old white native fireman entered the hospital with the complaint of weakness, dyspnea on exertion, and paroxysmal nocturnal dyspnea of five weeks' duration.

He had been perfectly well up until five weeks before entry, when quite unexpectedly he vomited shortly after his breakfast. He began to tremble all over, perspired profusely, had marked shortness of breath, and for a few minutes could not talk. The attack gradually subsided during the next half hour. However, about half an hour later, while walking, he had another attack of very severe shortness of breath. From that time until entry to the hospital he noticed increasing weakness and fatigue, increasing dyspnea on exertion, and definite attacks of paroxysmal nocturnal dyspnea which wakened him from sleep. He even had some dyspnea while lying in bed propped up on two pillows and discovered that he was most comfortable lying on one side partially supported by his arm. He had a slight cough, productive of small amounts of mucoid sputum. On the day before entry he noticed swelling of his ankles for the first time. His appetite remained fairly good, but it was such an effort for him to go to the restaurant where he had his meals that he ate less often and consequently had lost some weight. He had had no chest pain, palpitation, hemoptysis, visual difficulty, headaches or nosebleeds. He had had nocturia — one to two times each night — for as long as he could remember, and six years before entry for a period of a month he had had nocturia two to five times each night. This was not accompanied by dysuria, hematuria or other urinary symptoms.

He had had uncomplicated scarlet fever as a child but no other diseases that he remembered. He had not had repeated sore throats or rheumatic fever. His father, mother, two brothers and a sister were all dead of causes unknown to the patient.

Physical examination revealed a well-developed man showing some evidence of weight loss. He was sitting up in bed in moderate respiratory distress. The fundi showed recent hemorrhages and thickening of the arteries. There was slight icterus of the skin, and telangiectasis of the cheeks. The heart was slightly enlarged to the left, and there was a loud, snapping aortic second sound. No murmurs were heard. The blood pressure was 260 systolic, 150 diastolic. There were rales at both lung bases and slight edema of the feet. The abdomen was negative.

The temperature was 99.5°F., the pulse 100. The respirations were 28.

The urine had a specific gravity of 1.020 with a slight trace of albumin but no cells or casts in the sediment. The blood showed a red-cell count of 4,130,000 with 85 per cent hemoglobin and a white-cell count of 11,000 with 83 per cent polymorphonuclears. The blood Hinton test was negative. The nonprotein nitrogen of the blood was 57 mg., the van den Bergh 1.0 to 1.5 mg., biphasic, and the protein 5.5 gm. per cent. The chlorides were equivalent to 102 cc. of N/10 sodium chloride. A Takata-Ara test on the blood serum was negative. An electrocardiogram showed abnormal T waves suggestive of myocardial damage.

He showed striking improvement merely on bed rest and had a marked diuresis even before digitalis was given. On the sixth day the nonprotein nitrogen of the blood was 44 mg. per cent and the van den Bergh was normal. The improvement continued for eight days when quite suddenly there was a striking change in his condition. His head was turned to the left, there was flaccid paralysis of the entire right side of his body, he was unable to talk, and there were left nystagmoid movements of his eyes. His reflexes were normal. The blood pressure was 290 systolic, 150 diastolic, the pulse 108. The respirations were 24. A lumbar puncture showed an initial pressure of 400 mm. of water, with normal pulse and respiratory oscillations. The spinal fluid was blood tinged and contained 1539 red cells per cubic millimeter. The systolic blood pressure remained at 290, and he died within half an hour.

Differential Diagnosis

Dr. Alfred Kranes: The facts presented lead so unescapably to a definite diagnosis that one is reminded a bit of the old adage that "things are not always what they seem." I do not see how one can reasonably escape the conclusion, however, that this patient suffered from generalized arteriolar disease, resulting in hypertension, and that he died as a result of these factors exerting their effect on his heart and finally his brain. The course of the disease from the first symptom to death was unusually short, but we can be reasonably sure that hypertension and arteriolar disease must have been present for some time before his first symptoms; just how long would be pure speculation.

The sudden onset with vomiting, trembling, perspiration and dyspnea is rather suggestive of the paroxysmal attacks of hypertension which occur with certain types of adrenal tumors, chiefly the paragangliomas; but from that point on nothing further is said about trembling, perspiring or vomiting in attacks, and the course is quite typical of gradually increasing left ventricular failure, with paroxysmal nocturnal dyspnea, the train of events which is so common in hypertensive heart disease. Except for the onset, therefore, there is little on

which to base a diagnosis of an adrenal tumor with paroxysmal hypertension. I mention this possibility chiefly because what I believe to be the diagnosis seems too obvious.

It is quite surprising that with such clear-cut evidence of left ventricular failure, the heart was not larger than indicated here. The examiner found the heart to be "slightly enlarged to the left," though no measurements are given and the electrocardiographic report makes no mention of left-axis deviation. I am inclined to believe that the heart was fairly large, the enlargement of course consisting chiefly of a hypertrophied left ventricle.

The course of this patient's disease fits better into our concept of so-called "malignant" than that of "benign" hypertension. The height of the blood pressure alone, especially the diastolic pressure, does not distinguish the two forms, although high diastolic pressures, such as found here, are much commoner in the malignant form. Rather, the youth of the patient and the very short course of the disease favor the diagnosis of malignant hypertension. There is, however, one atypical feature. Unlike benign hypertension, in which heart failure is the commonest cause of exitus, in the malignant form it is the least common, renal failure being primarily responsible for most of the deaths. In this particular case there is not a great deal of evidence of impaired renal function, although admittedly the information is very scant. We have a single urine report with a specific gravity of 1.020 and two nonprotein nitrogens both of which are above normal. The latter could be solely the result of congestive heart failure, which the patient obviously had on admission, and the lowering of the nonprotein nitrogen with concomitant improvement of his heart failure suggests that the apparent renal failure was due to passive congestion of his kidneys. Since the patient died before adequate renal function studies could be done, — and these could profitably be done only after his cardiac failure was relieved, — we can only speculate about the condition of his kidneys. Since a large majority of patients with malignant hypertension have some renal involvement, we may venture a guess that some degree, at least, of necrotizing arteriolitis will be found, perhaps even a considerable amount; for had his life not been suddenly terminated by a cerebral hemorrhage, he might have died in uremia within the next six months or year. There is the possibility, of course, that this patient's hypertension was due to renal ischemia at a point proximal to the kidney itself, narrowing of the renal arteries, or arteriosclerotic plaques in the abdominal aorta at the mouths of the renal arteries, thereby causing a diminution of the renal blood flow. Since Goldblatt et al.[1] have pointed out the importance of renal blood flow in the production of experimental hypertension, cases of hypertension in which narrowing of the large renal vessels occurred have been noted. I know of no way of making such a diagnosis clinically, but mention it as an interesting possibility.

The terminal event was an obvious cerebral hemorrhage, the result of arteriolar disease plus hypertension.

In conclusion, therefore, I should say that this patient suffered from malignant hypertension, with the usual pathologic changes associated with this disease, namely hypertensive heart disease, some degree of renal involvement, cerebral arteriosclerosis and finally a cerebral hemorrhage.

Clinical Diagnoses

Malignant hypertension.
Cerebral hemorrhage.
Congestive heart failure.

Dr. Kranes's Diagnoses

Malignant hypertension.
Nephrosclerosis, malignant type.
Hypertrophy of the heart.
Cerebral arteriosclerosis.
Cerebral hemorrhage.

Anatomical Diagnoses

Nephrosclerosis, malignant type.
Arteriosclerosis, cerebral.
Cerebral hemorrhage.
Hypertrophy of the heart.
Pulmonary hyperemia and edema.

Pathological Discussion

Dr. Tracy B. Mallory: At not too infrequent intervals I find it a highly salutary measure to introduce in these clinics a perfectly obvious textbook type of case. I do it always, however, with a certain amount of trepidation since I have found that the psychological hazards are so great that the discusser is more than likely to "come a cropper." Dr. Kranes fortunately had the courage of his convictions and stuck to the obvious diagnosis. There was one additional clinical point which I thought he might have brought out in his discussion. In attempting to assess the amount of renal failure I should have put considerable weight on the fact that there was no significant grade of anemia. The blood level is, to my mind, one of the most reliable signs of renal insufficiency in the hypertensive case.

The autopsy showed, as Dr. Kranes predicted, a considerably larger heart than the physical ex-

amination indicated. It weighed 500 gm. and showed hypertrophy of both the left and right ventricles, so there was no particular reason for an axis deviation in the electrocardiogram. The kidneys were distinctly small for a man of his size, since they weighed only 225 gm. The capsules stripped with some difficulty, and the cortical surfaces were granular. On microscopic examination marked arteriolar changes were found in both the minute and the larger arterioles. In many of the latter the proliferative intimal thickening, often spoken of as endarteritis and characteristic of the malignant in contrast to the benign type of nephrosclerosis, was evident. There were numerous foci of glomerular and tubular destruction, but little or no compensatory tubular dilatation. This, I think, is important in clinicopathological correlation since Kimmelstiel and Wilson[2] showed — and our own experience checks the point — that tubular dilatation is the most reliable histologic sign of functional renal impairment. The other noteworthy findings were limited to the central nervous system. The basilar and cerebral arteries showed moderate to severe arteriosclerosis. An extremely large hemorrhagic cavity containing about 70 cc. of fluid and clotted blood was found in the left cerebral hemisphere. It extended from the frontal lobe backward to the occipitoparietal region. It had ruptured into and was continuous with the left ventricle, and fluid blood was found in all the other ventricular cavities as well.

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GROUP HOSPITAL INSURANCE

An increasing number of persons are availing themselves of some form of insurance whereby, for a modest sum, the assured may be entitled to a limited amount of hospitalization each year for every member of his family. Under the terms of the Associated Hospital Service Corporation of Massachusetts, for instance, the policyholder is allowed twenty-one days of hospital care in a semi-private room, together with general nursing service, routine medication and "routine laboratory or pathological service as usually offered to the individual patient by the particular hospital to which the patient goes." That the general public, by and large, benefits from such arrangements is beyond question. That is as it should be. From various quarters, however, objections have arisen concerning the amount and character of the service rendered.

The American Medical Association* has adopted the principle that "the benefits shall be paid in cash directly to the member," in order "that he may purchase his own medical [professional or hospital] service from whatever source he may desire." "When the individual himself pays for the services he receives," says the association, "he can be assured of adequate and satisfactory services; otherwise he can refuse to make payment." There is, however, no implication in the accepted forms of insurance that the patient is not free to choose his physician or surgeon other than that he must be a staff member of one of the hospitals participating in the insurance plan. If there is a choice of laboratory physicians in the member hospital, — there rarely is even in the larger hospitals, — it is unlikely that the patient would be capable of making a choice advantageous to himself. Furthermore, the adoption of cash payments would require, according to law, the establishment by the issuing company of a cash reserve, and thus the cost of insurance would be notably increased thereby defeating, in part at least, the very purpose for which the plan was created. Such policies would differ but little from the health insurance that companies organized for profit have for many years offered with but scant interest on the part of the general public. For this type of insurance, we cannot sympathize with the principle of cash payments to the assured.

From a number of sources, including the association, has come the view that the assured's benefits should be confined to "hospital accommodations such as room, bed, board, operating room facilities and the general nursing care ordinarily provided by hospitals," and that the services of "physicians, either general or special," be excluded. A separate professional charge, therefore, would be made for each and every laboratory procedure and these charges would, in no sense, be covered by the insurance.

Hospital service, however, should never interfere with the existing relation between the physician and the hospital or between the physician and the

*Editorial: The roentgenologist, the pathologist and the anesthetist under hospital insurance plans. J. A. M. A. 111:158, 1938.

patient. These relations differ in various regions and in various hospitals. No one insurance plan, therefore, can properly be applied to all hospitals or to all localities.

It would seem more equitable to all concerned to offer to the assured those services which, in the hospital that he enters, would be available were he not insured. If the relation between, let us say, the pathologist and the hospital be such that he is paid a full-time salary and in return performs all necessary and routine pathological examinations without further charge, such an arrangement should still obtain whether an entering patient be insured or not. Neither the hospital nor the patient nor the pathologist would be exploited, the patient would be protected and no loss would accrue to either the physician or the hospital. Such has been proved to be a fact. If however, as in a smaller hospital, the pathologist be on a "piece work" basis,—if the local arrangement be such that he is paid for each examination,—then the assured would be required to pay cash for an examination done by him, for it would not be "routine." Again the existing relations would be undisturbed. No ethical or legal principle would be violated.

In either instance, moreover, if the pathologist were called to observe an operation or to do a frozen section, such an act on his part would constitute a consultation, and he would, whether the patient were insured or not, be entitled and expected to charge an appropriate fee.

By confining the assured's benefits to "routine examinations,"—and each hospital with the approval of its constituent staff would determine what should be regarded as routine,—the patient would receive adequate protection, and neither the physician nor the laboratory worker nor the hospital would be the loser. In such a case, the primary object of the hospital—to provide all the services necessary for the diagnosis, treatment and rehabilitation of the patient—would be upheld, neither law nor local custom would be infringed on and the general public would be protected—as it should be.

POSTMORTEM EXAMINATIONS

THE address by Dr. Alan Gregg to the American College of Physicians entitled "A Broader View of Postmortem Examinations," which appeared in the August number of the *Annals of Internal Medicine,* contains an important message, not only to every practitioner of medicine but also to every layman.*

Dr. Gregg's chief point, if we read him aright, is that instead of a situation in which the doctor is obliged to beg the family for a postmortem examination, we ought to have one in which the family (or even the patient) demands that such an examination be made. And the reason for this is that the doctor, being human, will be less on his mettle to give the best that is in him in the way of service if he can comfortably bury his mistakes than if he knows that the denouement of a postmortem lies ahead.

The postmortem is the most powerful stimulus to high professional endeavor that exists. When the layman learns this, he will realize that in granting permission for a postmortem he is not simply obliging the doctor but serving his own interests as well. And so Dr. Gregg concludes: "Because it is in the interest of the patient, the postmortem can change gradually from being hated and feared and avoided to being used and trusted and steadily perfected."

*For the benefit of those physicians who wish to distribute copies of this address among their patients it should be noted that, in an editorial (Postmortem Examinations, Ann. Int. Med. 12:268,1938) commenting on Dr. Gregg's paper the statement appears that "arrangements have been made . . . whereby any practicing physician can order . . . reprints direct from the Lancaster Press, Lancaster, Pennsylvania."

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SPONTANEOUS RUPTURE OF UTERUS AND BLADDER DURING LABOR

Mrs. M. B., aged twenty-eight, a Russian primipara, was delivered at home on July 15, 1921, by low forceps after twenty-one hours of labor.

A series of selected case histories by members of the section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the section.

At the time of delivery, the cervix was fully dilated and the head was on the perineum. Bloody urine was obtained by catheter prior to the operation. The baby, a stillborn infant, whose weight was not recorded, was delivered easily and the placenta followed immediately. A second-degree laceration of the perineum was routinely repaired. Following recovery from the anesthetic, the patient complained of tenderness in the left lower abdominal quadrant and in the left costovertebral angle. Abdominal distention rapidly developed. The morning after delivery the temperature was 98.4°F., and the pulse rate 104. Three hundred cubic centimeters of bloody urine were obtained by catheterization. Two days after delivery the patient was incontinent, and bloody urine was running from the vagina. There was slight fullness in the left flank; the temperature was 97.0°F., and the pulse rate 100. She was transferred to the hospital.

The family history was entirely negative. The patient had always been well. There had been no operations. Catamenia began at thirteen, were regular with a twenty-eight-day cycle, and lasted five days. Her last period begin on October 7, 1920, making her expected date of confinement July 14.

Physical examination revealed a somewhat apprehensive woman complaining of abdominal distress. The tongue was coated and slightly dry. The heart was not enlarged, and the sounds were regular and of good quality; the rate was 110. The chest showed normal expansion, the lung fields were clear, and the respiratory rate was 18. Examination of the abdomen revealed a firm mass in the right lower quadrant thought to be the uterus. There was a softer mass in the left flank over which there was considerable tenderness. A catheter was introduced into the urethra, and a small amount of bloody fluid was obtained. The same type of bloody fluid was leaking from the vagina. The lochia was bloody but not foul. The lower extremities were not remarkable, and the reflexes were equal and active.

On the day following entry the temperature was 98.2°F., and the pulse 100. The abdomen was more distended than previously, and the patient was still incontinent. A vaginal examination revealed a tear in the center of the anterior cervical lip which extended to the anterior vaginal wall. It was possible to insert the examining finger through the rent into the bladder and palpate a catheter which had been inserted through the urethra.

On July 19 a genitourinary consultant confirmed the diagnosis of vesicovaginal fistula and advised against operative interference at that time. She then had a rising temperature and pulse rate. She died on the following day.

Autopsy showed the anterior wall of the uterus to be torn upward from the cervix for a distance of 11 cm. The rent was to the left of the midline and communicated with the cavity formed by the separation of the layers of the broad ligament and with the bladder. The anterior wall of the vagina presented an opening, 1 cm. in diameter, just superior to the cervix, which communicated with the bladder. The pelvic mass and retroperitoneal cavity contained bloody urine and showed evidence of infection.

The summary of the pathological report was as follows: "The pelvic mass and continuous retroperitoneal cavity contained fluid which, though blood-tinged and turbid, was evidently urine. The walls of this cavity presented the characteristic appearance attending extrinsic urinary extravasation accompanied by infection. This extrinsic extravasation implies a rupture of the bladder at a time preceding delivery, otherwise escape of urine would have occurred through the channels revealed by the examination of the pelvic organs. It seems improbable that the opening in the bladder, because of its nearly circular shape and restriction to the region of the trigone, could have been caused by a sudden application of force. A hematoma must have existed, and the bladder communication was probably established by necrosis of the bladder wall subsequent to the hematoma and by pressure. This hematoma very likely arose from a tear in the uterus at the cervix."

Comment. Spontaneous rupture of the uterus during labor is not often recognized unless associated with hemorrhage or the symptoms of collapse. While this rupture as it extended into the bladder was the cause of death from peritonitis, it was not associated with hemorrhage, and had it not gone into the bladder, might never have caused symptoms severe enough to suggest that rupture had occurred. It seems quite likely that this patient must have been fully dilated a good many hours and that pressure necrosis was the cause of the rupture. It is very difficult to see how a simple low forceps, as so described, to a head on the perineum could have done any mechanical damage. Had the rupture of the bladder been diagnosed earlier than it was, it is questionable whether anything else could have been done. Most spontaneous ruptures of the uterus occurring during labor are preventable. If pressure resulting in necrosis was the cause of this rupture, earlier delivery would have prevented it.

DEATH

COLBY — FRED B. COLBY, M.D., of 131 Pearl Street, Gardner, died October 6. He was in his sixty-ninth year.

Born in Andover, Maine, he was graduated from Hebron Academy and received his degree from Dartmouth Medical School in 1896. He began practice in Highland Falls, New York, and later went to Rangeley, Maine. He had practiced in Gardner for thirty years. Former city physician of Gardner he was also a member of the Board of Health from 1920 to 1932. Dr. Colby was a past president of the staff association of the Henry Heywood Memorial Hospital. He was a fellow of the American Medical Association and a member of the Massachusetts Medical Society.

His widow, two sons, two daughters, his mother and a sister survive him.

MISCELLANY

"YOUR HEALTH" BROADCASTS

A new series of dramatized health broadcasts, titled "Your Health," is being prepared this year by the American Medical Association and the National Broadcasting Company. The broadcasts consist of thirty-minute dramatizations, written and produced by professional radio artists, with orchestral accompaniment. Each skit is prepared on the basis of information furnished by the Bureau of Health Education of the American Medical Association and is intended to supplement, dramatize and enrich health instruction in the schools, but not to take the place of classroom instruction, textbooks or project teaching.

The program will be broadcast over the Blue Network of the National Broadcasting Company each Wednesday at 2:00 p. m., Eastern Standard time, beginning October 19. The first series, titled "Personal Health," consists of four broadcasts, as follows:

October 19. What Is Health?
Introductory: explanatory.

October 26. Growing Strong.
Favorable and unfavorable factors in growth and the maintenance of normal weight.

November 2. Seeing and Hearing Well.
Hearing and vision; how to conserve these; how to recognize deviations; how to prevent loss.

November 9. Healthier Boys and Girls.
So-called physical defects; their recognition; what can be done about them.

ASSOCIATED HOSPITAL SERVICE

The Blue Cross of Massachusetts completed its first year of operation on October 1. More than 82,000 employed persons and their dependents were enrolled for membership, and $152,000 was paid to member hospitals for service to subscriber patients during the year. "The non-profit plan for hospital care in Massachusetts is now fourth largest among 40 similar associations in this country, and is larger than any of the units established during the past two years," R. P. Cahalane, executive director of the service, said. "It is the only organization in the state of its kind and one of four in the United States to provide a state-wide service."

"The people of Massachusetts have been quick to take advantage of this easy method of paying for hospital bills, as evidenced by our enrollment figures," he added. "Our list of member hospitals, numbering 123 and representing almost every general hospital in the State eligible for membership in this service, is second in number only to New York City, and second to none in equipment, personnel and administration, with outstanding men of the medical profession included on the staffs. Associated Hospital Service in New York City enrolled 86,000 subscribers the first year of operation. Now in its fourth year, it has a membership of 1,000,000, almost half the total of those enrolled in similar organizations in the United States. Hospital authorities estimate that 10,000,000 citizens and their dependents will be enrolled in non-profit hospital-service associations by 1940."

Two branch offices have been established in Massachusetts to facilitate enrollment: the first at New Bedford in February and the second at Worcester in May. Further expansion will include a third branch at Lowell and a fourth at Springfield in the near future, it was announced.

About 1500 Massachusetts physicians and surgeons have attended Blue Cross patients in hospitals during the year. The medical profession receives no fees from the Blue Cross; each subscriber makes payment direct to his attending physician for professional services, according to George Putnam, president of the service.

"However, the attending of subscribers in our participating hospitals has given these doctors a better understanding of the service and how it operates for their benefit in that it pays the hospital bill and leaves the subscriber his own funds to pay the doctor," Mr. Putnam explained. "We are well pleased with the year's progress, and I predict that at least 150,000 residents of Massachusetts will be enrolled in this community co-operative project by January 1. Massachusetts hospitals, always in the forefront of progress, are to be commended for their ready and whole-hearted co-operation in establishing this service."

The subscriber selects his own physician and makes payment direct to him for professional services. The relation between doctor and patient and between the doctor and the hospital is not altered in any way. The Blue Cross operates without profit and without charity and is tax-exempt. Its main purpose is to provide low-cost hospital care for the moderate-income group. Secondarily, member hospitals benefit in the form of full and prompt payment for service to subscriber patients. No commissioned solicitors are employed, and no money is spent in advertising. The officers and directors, who serve without compensation, are as follows: George Putnam, president; Dr. Nathaniel W. Faxon, vice-president; Frederick W. Ayer, Rev. Robert P. Barry, Dr. J. Harper Blaisdell, Edward Dana, Dr. Channing Frothingham, Louis E. Kirstein, Horace Morison and Alexander Wheeler, directors.

NOTES

Dr. Richard P. Strong, professor of tropical medicine at Harvard Medical School since the founding of the department in 1913, has retired from active teaching to become professsor emeritus. His place has been taken by Dr. John E. Gordon. Dr. Gordon received a Ph.G. degree from Northwestern University in 1913 and in 1916, 1921 and 1924 was granted M.S., Ph.D. and M.D. degrees respectively by the University of Chicago. For the last four years he was a member of the International Health Division of the Rockefeller Foundation.

Middlesex University School of Medicine announces the appointment of Dr. Josef Fischer, formerly of Vienna, as a full-time professor of otolaryngology. Dr. Fischer received his medical degree from the University of Vienna in 1915, serving as private assistant to Professor Politzer and auditor under Professor Neumann in the Department of Otology. After four years of service in the World War, he be-

came the assistant of Professor Alexander in the Department of Otology and of Dr. Kaiser in the Department of Laryngology. In 1933 he became the first assistant to Dr. Brunner, and substituting director at Dr. Brunner's ear, nose, and throat clinic in Vienna; and in 1934 he was made a member of the teaching staff of the American Medical Association of Vienna. In 1938 he was elected vice-president of the Austrian Otolaryngological Society.

CORRESPONDENCE

MICHELANGELO'S LAMENT

To the Editor: The following is from *Michelangelo, The Man* (New York City: Tudor Publishing Company, 1936), by Donald Lord Finlayson.

At the time of writing the poem, Finlayson tells us, Michelangelo was engaged in painting the vault of the Sistine Chapel, over which he worked for ten months, like a galley slave, without assistance. Finlayson adds that to get an idea of what the artist suffered:

> One need gaze only an hour at the Sistine vault, and then, nursing a lame back reflect what it might mean to be caged for months in the dark, cramped area between the vault and the huge vault-shaped platform, just arm's length below it, lying on one's back, crawling about with paint dropping in one's face, straining one's eyes out of their sockets to see the damp plaster above in the half-gloom. No solitary cell in any penitentiary could be more terrible than this.

The poem is as follows:

I've grown a goiter by dwelling in this den —
As cats from stagnant streams in Lombardy,
Or in what other land they hap to be —
Which drives the belly close beneath the chin.
My beard turns up to heaven, my nape falls in,
Fixed to the spine; my breast bone visibly
Grows like a harp; a rich embroidery
Bedews my face from brush-drops thick and thin.
My loins into my paunch like levers grind:
My buttock like a crupper bears my weight,
My feet unguided wander to and fro;
In front my skin grows loose and long; behind,
By bending it becomes more taut and strait;
Crosswise I strain me like a Syrian bow;
Whence false and quaint I know
Must be the fruit of squinting brain and eye;
For ill can aim the gun that bends awry.
Come, then, Giovanni, try
To succour my dead pictures and my fame,
Since foul I fare and painting is my shame.

Notwithstanding Michelangelo's misgivings, we are told that at this time the part completed "was immediately and unanimously acknowledged as the greatest achievement in painting so far seen in Rome."

This lament was in all probability written in the winter of 1508-09, and Michelangelo's reference at that time to his goiter and the goiters of cats who drank "from stagnant streams in Lombardy," gives the poem additional interest.

William Pearce Coues, M.D.

12 Monmouth Court,
Brookline, Massachusetts.

REPORT OF MEETING

NEW ENGLAND OTOLOGICAL AND LARYNGOLOGICAL SOCIETY

A meeting of the New England Otological and Laryngological Society was held at the Massachusetts Eye and Ear Infirmary, Boston, on February 16, 1938. The following program was presented:

Serous Labyrinthitis. Dr. Harry Butler, Bangor, Maine.

The author studied 16 cases of serous labyrinthitis over a period of nine and a half years. The ages of the patients ranged between forty-five and sixty years. None of the cases fulfilled the postulates of Ménière's disease.

Since the author regards this type of labyrinthitis as a hyperemia and serous inflammation of end organs, he devised a method of treatment by means of which the end organs in question were put at rest. For a period of three weeks the patients were put to bed flat on their backs, with only a small pillow. They were not allowed to move their heads. At the same time, dehydration was accomplished by a preliminary catharsis, pilocarpine by mouth and limitation of the fluid intake. Since nearly all cases had some inflammation of the eustachian tube, with decreased patency, periodic inflation of the tube and shrinking of the nasal mucosa were carried out. After the treatment had been terminated, the patients were gradually allowed to increase their activities, until in six weeks they were normal.

Discussion. Dr. Moses H. Lurie (Boston) said that he regards the treatment by immobilization as entirely rational. He has, however, given up the administration of pilocarpine as being of no particular help.

The Surgical Treatment of Chronic Dacryocystitis. Dr. Samuel W. Garfin, Boston.

After outlining the history of the treatment of chronic dacryocystitis, the indications for the West operation were cited. The author uses the transseptal route. The right tear sac is approached through an incision of the septum from the left vestibule, and vice versa. The incisions on both sides of the septum are made in such a way that they do not lie in the same plane, in order to avoid a permanent perforation. In this manner the operative field is brought into better view and the technical difficulties encountered by the approach through the same side are greatly eased.

Twenty-eight operations were performed by this method over a period of twelve years. The greater number of these patients could not be followed up to date and so no statistical data were presented. However, Kofler was cited as having had approximately 90 per cent cures in many hundreds of these operations over a period of some twenty years.

Discussion. Dr. Charles T. Porter (Boston) doubted that the author's method offers any advantages over the Mosher-Toti operation except the possible lack of an external scar. On the other hand he said that the intranasal route offers a great many more difficulties especially in cases that have to be operated on again.

Dr. Garfin admitted the difficulty of an eventual reoperation. He claimed, however, that the external operation necessitates a disarrangement of the structures in the region of the external canthus with a possible resulting impediment of tear flow into the nose. He added that the transseptal operation facilitates the approach to the anterior ethmoidal cells, suppuration of which is regarded by some as an etiologic factor in chronic dacryocystitis.

UNDIFFERENTIATED NEOPLASM OF THE THYROID AND LARYNX WITH MULTIPLE METASTASES. Dr. Andrew L. MacMillan, Jr., Concord, New Hampshire.

Case report. The patient was a sixty-three-year-old man, whose chief complaint was pain in the left side of the neck and increasing hoarseness. When first seen several weeks after the onset there was a slight enlargement of the left lobe of the thyroid. Biopsy taken from the thyroid was diagnosed as chronic thyroiditis and adenoma of the thyroid. The larynx showed no remarkable changes at this time. Two months later a small mass was seen on the anterior wall of the trachea. Biopsy from this was diagnosed as epidermoid carcinoma (Grade III). A month later the patient died of a bronchopneumonia. Autopsy showed the primary growth to be in the thyroid, with secondary invasion of the larynx. There were metastases in the pericardium, heart, pleura, lungs, kidneys, adrenals and pancreas.

PRELIMINARY STUDIES OF THE BLIND SPOT IN HEAD INJURIES. Dr. Howard F. Hill, Waterville, Maine (by invitation).

The value of complete visual-field studies in cases of head trauma has long been known, whereas but little attention has been paid to the blind spot and its changes in such injuries.

In all cases of major or minor head injuries a careful daily check should be kept of changes in the contour and size of the blind spot. A persistent increase in its size indicates severe trauma and probably some increased intracranial pressure or edema. Its changing contour often gives an accurate index of the rise and fall of intracranial pressure from day to day. In this respect it is a far more sensitive indicator than either the peripheral field or the nerve head.

The author examined the blind spots of college boys after boxing bouts with light-weight gloves. Two or three minutes after having received blows on the head severe enough to cause temporary vertigo, the blind spots of the boxers were charted and the fundi examined. In all such cases enlarged blind spots were found. They persisted for from three to fifteen minutes and then gradually returned to normal. At the same time the fundi remained normal throughout.

NOTICES

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

The next meeting of the Boston Society of Psychiatry and Neurology will be held at the Boston Medical Library, Thursday evening, October 20, at 8:15.

PROGRAM

The Cerebrospinal Fluid in Retrobulbar Neuritis. Dr. A. L. Watkins (by invitation).

Observations on Spastic Paralysis and Dystonia Musculorum Deformans. Dr. M. S. Burman (by invitation).

E. HOUSTON MERRITT, M.D., *Secretary.*

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The first fall meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday evening, October 19. The council will meet at 6:00, and dinner will be served at 6:30. The program will begin at 8:00.

Dr. William H. Watters will speak on "Physical Medicine in Chronic Disease." Discussion by Dr. DeWitt G. Wilcox, of Newton, and Dr. George E. Percy, of Salem, will follow.

All members of the medical profession are cordially invited to attend.

WILLIAM D. MCFEE, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, October 25, in the Peter Bent Brigham Hospital amphitheater (Shattuck Street entrance), at 8:15 p. m. Dr. Channing Frothingham will preside.

PROGRAM

Presentation of cases.

Certain Cardiorenal Circulatory Correlations. Dr. Henry A. Christian.

Medical students and physicians are cordially invited to attend.

ROBERT ZOLLINGER, M.D., *Secretary.*

BOSTON CITY HOSPITAL

The monthly clinicopathological conference will be held at the Boston City Hospital on Wednesday, October 19, at 12 o'clock noon in the Pathological Amphitheater.

JOSEPH E. HALLISEY, M.D., *Secretary,*
Medical Staff.

NEW ENGLAND SOCIETY OF PSYCHIATRY

A semi-annual meeting of the New England Society of Psychiatry will be held at the State Hospital for Mental Diseases, Howard, Rhode Island, on Tuesday, October 18. The hospital will be open for inspection from 9:00 a. m. to 4:00 p. m., and the dedication exercises in connection with the opening of the new psychiatric clinic building, named in honor of Dr. Adolph Meyer, of Baltimore, will begin at 10:00 a. m. The address of the day, "The Psychiatric Hospital in a Progressive Health Program," will be given by Dr. Meyer. Members of the Society are requested to bring only those guests whose interest is professional.

NEW ENGLAND HEART ASSOCIATION

There will be a meeting of the New England Heart Association in conjunction with the Suffolk District Medical Society at the Boston Medical Library, Wednesday, October 26, at 8:15 p. m.

Dr. G. E. Hall, of the Banting Institute and of the Department of Medical Research, University of Toronto, will speak on "Neurogenic Influences in Experimental Coronary Artery Disease."

Interested physicians and medical students are invited to attend.

EDWARD F. BLAND, M.D., *Secretary.*

CAMBRIDGE HOSPITAL

The regular clinicopathological meeting of the staff of the Cambridge Hospital will be held at the hospital, 330 Mt. Auburn Street, Cambridge, on Tuesday, October 18, at 8:30 p. m.

Dr. William Dameshek will speak on "Acute Hemolytic Anemia." All members of the medical profession are cordially invited to attend.

STEPHEN M. BIDDLE, M.D., *Secretary.*

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, October 17

Tuesday, October 18

*9-10 a. m. Boston Dispensary. Clinicopathological conference. Dr. R. C. Wadsworth and Dr. William Dameshek.

9:30 a. m. Massachusetts General Hospital. Thoracic clinic. Ether Dome.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

*12 m. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

Wednesday, October 19

8 a. m. Massachusetts General Hospital. Grand rounds. Orthopedic Department.

*9-10 a. m. Boston Dispensary. Hospital case presentation. Dr. S. J. Thannhauser.

*12 m. Clinicopathological conference. Children's Hospital amphitheater.

12 m. Boston City Hospital, conference on clinical pathology. Pathological amphitheater.

3 p. m. New England Dermatological Society. Massachusetts General Hospital

*8 p. m. New England Society of Physical Medicine. Hotel Kenmore.

Thursday, October 20

8 a. m. Massachusetts General Hospital. Circulatory clinic rounds.

*9-10 a. m. Boston Dispensary. The Mechanism of Rupture of the Graafian Follicle. Dr. J. T. Smith.

*10:30 a. m. Psychiatric Rounds. Boston City Hospital. Rounds will start at Room 916 on the ninth floor of the Medical Building.

11 a. m. Massachusetts General Hospital. Medical grand rounds.

12 m. Massachusetts General Hospital. Clinicopathological conference.

8:15 p. m. Boston Society of Psychiatry and Neurology. Boston Medical Library.

Friday, October 21

*9-10 a. m. Boston Dispensary. The Immediate and Ultimate Prognosis of Heart Disease. Dr. P. D. White.

10 a. m. Massachusetts General Hospital. Fracture rounds.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital, Ether Dome.

Saturday, October 22

*9-10 a. m. Boston Dispensary. Hospital case presentation. Dr. S. J. Thannhauser.

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.

October 17, 1938 and February 20, 1939 — American Board of Internal Medicine, Inc. Page 216, issue of August 11.

October 17-21 — Clinical Congress of the American College of Surgeons, New York City.

October 18 — South End Medical Club. Page 544, issue of October 6.

October 18 — New England Society of Psychiatry. Page 588.

October 18 — Cambridge Hospital. Page 588.

October 19 — Boston City Hospital, conference on clinical pathology. Page 588.

October 19 — New England Society of Physical Medicine. Page 588.

October 19 — New England Dermatological Society. Page 544, issue of October 6.

October 20 — Boston Society of Psychiatry and Neurology. Page 588.

October 24-26 — Academy of Physical Medicine, Scientific Session. Washington, D. C.

October 24 - November 4 — Graduate Fortnight of the New York Academy of Medicine. Page 181, issue of August 4.

October 25 — Harvard Medical Society. Page 588.

October 25-28 — American Public Health Association. Page 321, issue of September 1.

October 26 — New England Heart Association. Page 588.

October 31, November 1, 2, 3 and 4 — Inter-State Postgraduate Medical Association. Page 451, issue of September 22.

November 5 — American Board of Obstetrics and Gynecology. Page 145, issue of July 28.

November 5, 1938; February 4, May 15 and 16, 1939 — American Board of Obstetrics and Gynecology. Page 451, issue of September 22.

November 10 — Pentucket Association of Physicians, 8:30 p. m., Hotel Bartlett, 95 Main Street, Haverhill.

November 15-16 — New England Postgraduate Assembly. Page vii, Advertising Section, issue of September 29.

March 27-31, 1939 — American College of Physicians. Page 36, issue of July 7.

May 7-15, 1939 — International Congress of Military Medicine and Pharmacy. Page 501, issue of September 29.

September, 1939 — Boston Psychoanalytic Institute. Page 450, issue of September 22.

District Medical Society

ESSEX SOUTH

November 2 — Beverly Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. John Homans. Subject: Clinical Forms of Thrombophlebitis with Especial Reference to the Prevention of Pulmonary Embolism.

December 7 — Salem Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speakers: Dr. Walter G. Phippen and Dr. Channing Frothingham. Subject: Economic Problems.

January 4 — Danvers State Hospital. Clinic at 5 p. m. Dinner at 7 p. m.

February 8 — Essex Sanatorium, Middleton. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. Edward Churchill.

March 1 — Lynn Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. John Rock. Subject: Endocrinology.

April 5 — Addison Gilbert Hospital, Gloucester. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. Ethan Allan Brown. Subject: Allergy.

May 10 — Annual meeting. Salem Country Club, Peabody.

BOOK REVIEWS

Injection Treatment of Varicose Veins and Hemorrhoids. H. O. McPheeters and James K. Anderson. 315 pp. Philadelphia: F. A. Davis Co., 1938. $4.50.

The first part of this book is devoted to the treatment of varicose veins by injection. In the early chapters, after dealing with anatomical and physiological considerations, the author discusses the direction of the blood flow in the deep, superficial and communicating veins, using the complicated classification of Berntsen. Evidence of the backward flow of the blood, as demonstrated by lipiodol injection, is very fully illustrated. In the chapter devoted to pathology the curious statement is made that a thrombophlebitis in the deep system of veins is more likely to develop in the presence of large varices than when such varices are absent, a statement decidedly at variance with clinical experience. The chapter devoted to varicose ulcer is illustrated by pictures of the most advanced lesions and, though it contains a discussion of differential diagnosis from syphilitic, tuberculous, rodent and trophic ulcers, altogether fails to mention the postphlebitic ulcer. It would seem as if the author failed to recognize the fact that ulcers which occur after deep thrombophlebitis are rather different in nature from the varicose sort.

As to surgical methods of treatment, the author properly points out that the mortality in radical operations for varicose veins is very much higher than that of treatment by injection, and like other enthusiasts for injection, he is utterly opposed to operative treatment, condemning the latter by standards, particularly in respect to recurrences and accidents, that are much higher than those he uses for evaluating treatment by injections pure and simple. After a brief discussion of the various available chemicals, in which he expresses his preference for a certain solution, he fully describes equipment and technic. This is decidedly the best part of the book. If the directions of the writer were more carefully followed, the number of successful treatments would be infinitely greater. The same may be said of the very exquisite directions for the ambulatory treatment of ulcer. As regards the results of his treatment of varices, doubtless the author succeeds in securing the cures pictured in his illustrations. However, few surgeons would expect to achieve permanent obliteration, by injection alone, of the enormous varices pictured on pages 127, 128 and 130. The author would have done well to state the elapsed period after treatment at which the photographs of the treated legs were taken.

The author devotes only four and a half pages to what he describes as "preliminary ligation combined with injection." Considering the number of responsible investigators who believe that reasonably permanent cures of good-sized varices cannot be secured without a thorough dissection and division of the vessels at the saphenous

opening, the failure to go carefully into the matter of such divisions seems inexcusable. There is not even an illustration of the technic of this procedure, nor is there any comparative account of the results when this procedure is or is not used.

In respect to complications, particularly pulmonary embolism, the author is, of course, correct in his statement that embolism from varicose veins is very infrequent, whether or not the treatment by injection is used. He rather naïvely attributes this freedom from embolism to the direction of the venous flow in varix, speaking as if the individual with varicose veins never lay down; whereas the very unhealthy state of the vein's wall is sufficient reason for the comparatively solid adhesion of the thrombus in the varicose vein, whether or not treated with sclerosing chemicals.

In the chapter "Causes of Failure in the Injection Treatment of Varicose Vein," the author describes the "percussion pulse transmitted" as an original observation. He might have recognized this very satisfactory method of tracing the course of the filled varicose veins as that described by Chevrier as the "signe de la chiquenande de Schwartz" and adapted by Homans to the upright position. He would also have done well to leave out his chapter "Elephantiasis and the Elephantoid State Due to Lymphatic Destruction." He seems to have confused the unusual type of elephantiasis associated with ulceration and infection with the not at all uncommon elephantiasis nostra which, of course, is not caused by any tropical disease and which occurs in many others than "in patients who have recently migrated from the source of infection."

Altogether, the part of the book devoted to varicosity is an extraordinary mixture of useful information about veins and varices, intelligently and fully described, together with the most effective methods using sclerosing solutions, and rather ill-considered statements about a number of matters with which the author seems not to be sufficiently familiar. It is unfortunate that in his account of results he fails to introduce authoritative figures of his own, relying on oft-quoted statements of astonishing results from foreign clinics.

The second half of the book is a very modest, brief, but full and satisfactory account of the injection treatment of hemorrhoids.

As a manual of the treatment of varicose veins by injection and as a source of useful information on the ambulatory treatment of varicose ulcer, Dr. McPheeters' section of this book can unreservedly be recommended. It is readable and clearly printed. The illustrations are excellently reproduced.

Diseases of the Thyroid, Parathyroids, and Thymus. André Crotti. Third edition, thoroughly revised and enlarged. 1229 pp. Philadelphia: Lea & Febiger, 1938. $20.00.

The third edition of this book brings up to date Crotti's experiences in his particular field, which are now based on about 18,000 nonsurgical cases of goiter and about 9000 cases in which thyroidectomy was performed.

An excellent survey of the fundamentals concerning diseases of the parathyroid glands and a brief review of the anatomy of the autonomic nervous system have been added to the text.

Crotti has always been partial to the infection theory as the cause of endemic goiter. His research work on "goiter fungus," started in 1910 and completed in 1933, is included in this review. Many will continue to disagree with his theory, but Crotti presents his work in detail.

The text is on the whole very complete and well presented; 977 pages are devoted to diseases of the thyroid gland, and 116 pages to the thymus. The illustrations, particularly the colored plates on operative technic, are excellent. The sections on the parathyroid glands, hypothyroidism, the symptomatology of toxic goiter, the historical aspects of goiter, including the Kocher-Raverdin controversy, and the water transmission of goiter are particularly satisfactory.

His conclusions in many instances seem dogmatic and based on his personal experiences. Many will disagree with some of his theories. There are omissions from the recent literature: for example, the use of A.T.-10 in the treatment of patients with postoperative chronic tetany; recent work on blood iodine in thyroid disease; modern advances in the field of anesthesia in thyroid surgery, such as the use of cyclopropane; and roentgen therapy in the treatment of patients with malignant diseases of the thyroid gland.

This book, however, is to be recommended and should be read by all interns and surgeons who are interested in this field.

A Textbook of Histology. Alexander A. Maximow and William Bloom. Third edition. 668 pp. Philadelphia and London: W. B. Saunders Co., 1938. $7.00.

It should be a matter of considerable importance to undergraduates, research students and practitioners of medicine that Professor Bloom has extensively revised his textbook. As in previous editions, physiologic data have been included when they have correlated with structure, as has pathologic material where it helps to explain normal function. All this has been accomplished in a decidedly readable style.

Many illustrations are new, and they have a certain freshness. Attention may be called, for example, to the excellent colored illustration on page 308 of the sections of human thyroid in exophthalmic goiter and colloid goiter; to the photograph on page 531 of the living human ovum; to the colored figure on page 208 illustrating the types of nerve endings; and to the several frames of a moving picture film on page 532 showing ovulation in the rabbit. It must be remarked that the figures throughout the book show judicious care in selection and skillful execution.

A selected list of references, which includes articles with extensive bibliographies and, in nearly every case, at least one important historical reference, follows each chapter. It appears certain that this textbook will be recommended by teachers in all medical schools either as a prescribed text or as a text for correlated reading, for it has already become one of the standard books of American histology.

Proceedings of the Fourth Conference on Psychiatric Education. 345 pp. New York: The National Committee for Mental Hygiene, Inc., 1938. $1.00.

This conference was held at the Johns Hopkins Medical School in April, 1936. Forty-two schools and twenty-two other organizations were represented. Expression was given by teachers of psychiatry in the leading schools of the country as regards their methods of presenting psychiatry, psychobiology and psychoanalysis to medical students. The notes are full, and the discussion ample. To medical educators, this is an invaluable compilation. Additional material on psychiatric problems in general supplement the educational data. It is a worthy record of a highly developed specialty. Most emphasis is given, wisely, to the psychiatric approach to general medicine; in that, lies the real value of this publication.